Mohamed
PCT/99/19066
09/763,559

Structure search limits have been increased. See HELP SLIMIT for details.

=> d l3 que stat;d l6 que stat

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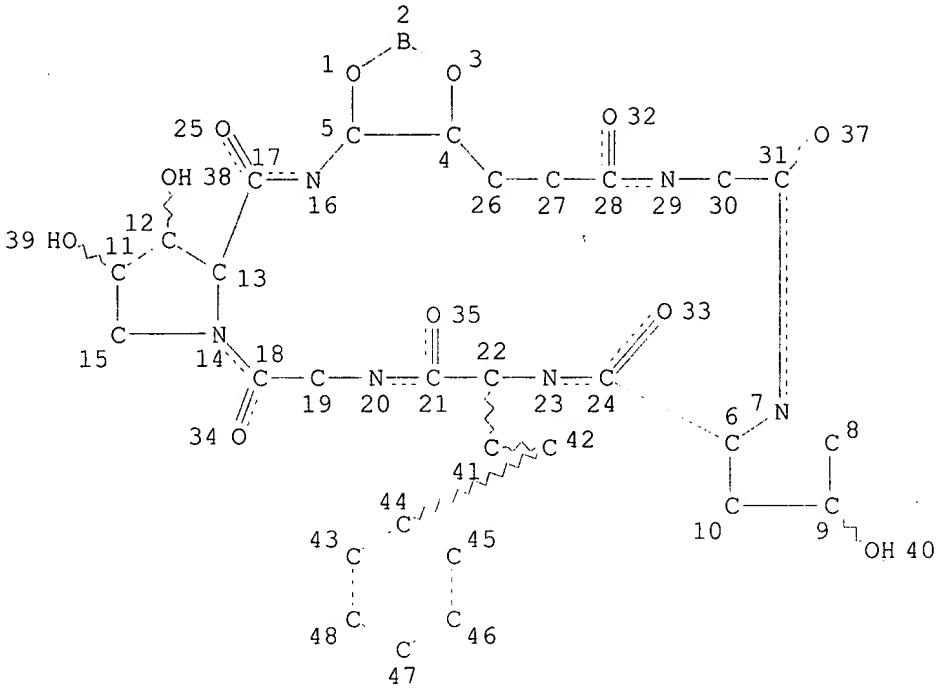

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DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
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NUMBER OF NODES IS 47

STEREO ATTRIBUTES: NONE
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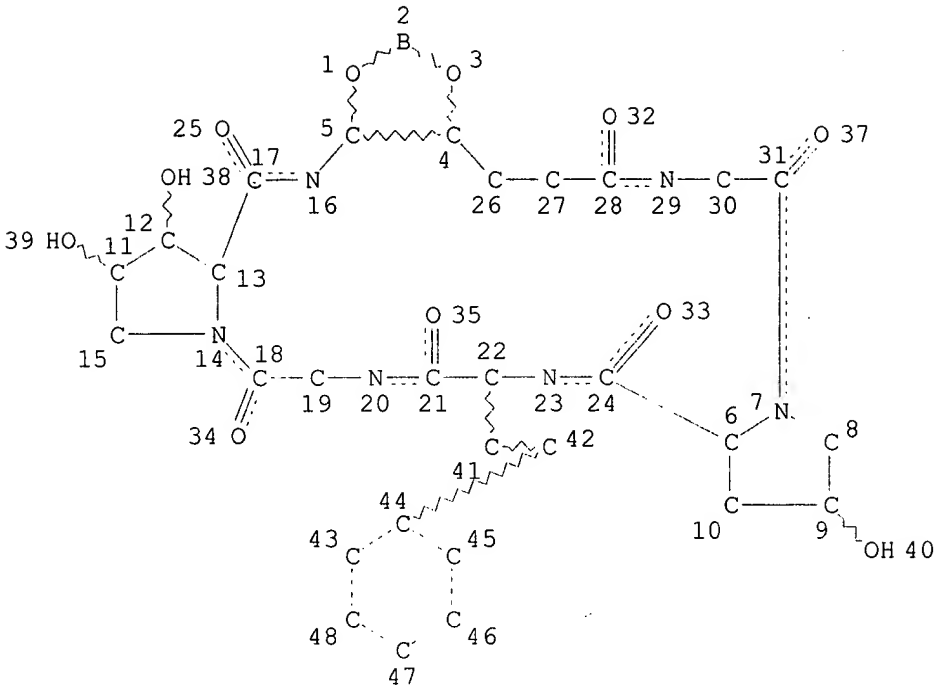

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GRAPH ATTRIBUTES:
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NUMBER OF NODES IS 47

STEREO ATTRIBUTES: NONE
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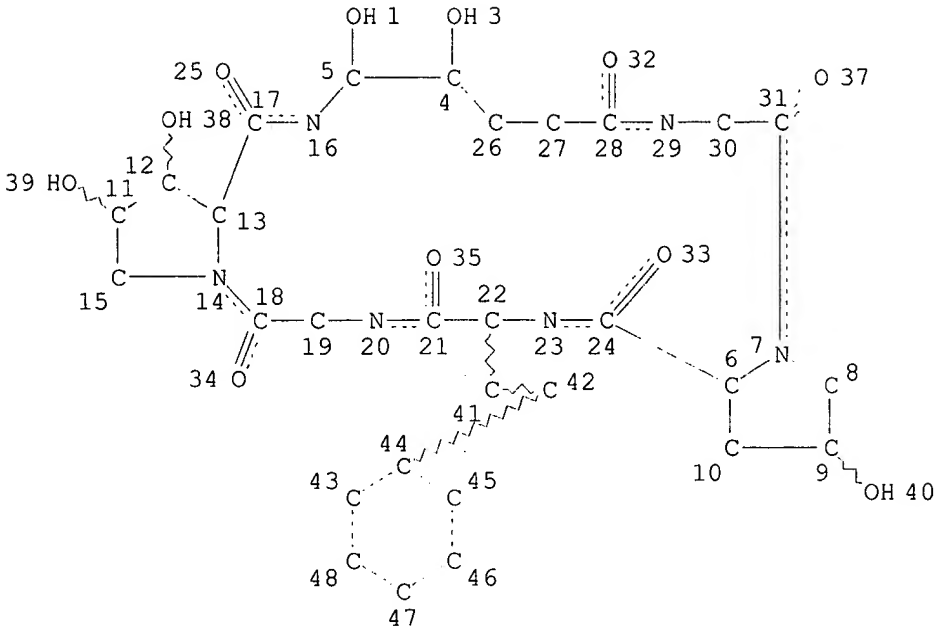

NODE ATTRIBUTES:
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DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 46

STEREO ATTRIBUTES: NONE
L9 14 SEA FILE=REGISTRY SSS FUL L7

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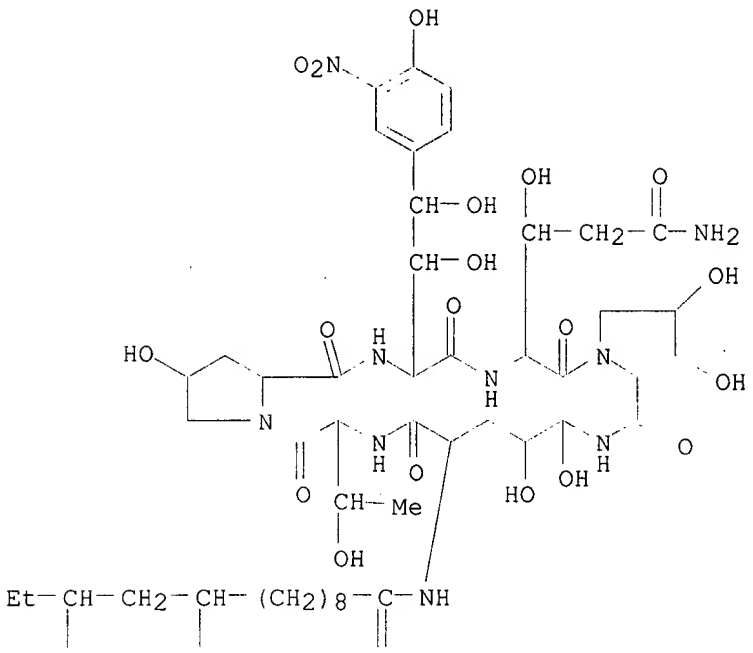
SEARCH TIME: 00.00.01

L9 ANSWER 1 OF 14 REGISTRY COPYRIGHT 2000 ACS
RN 173305-74-3 REGISTRY
CN Pneumocandin D0,
4-[(S)-4-hydroxy-4-(4-hydroxy-3-nitrophenyl)-L-threonine]-
(9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE; STEREOSEARCH
MF C50 H79 N9 O20
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

PAGE 1-A



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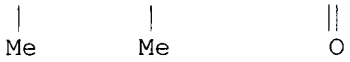


1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 124:146869 Preparation of cyclopeptide antifungal and anti-pneumocystis compounds.. Balkovec, James M.; Bouffard, Frances Aileen; Black, Regina M. (Merck and Co., Inc., USA). PCT Int. Appl. WO 9527074 A1 19951012, 81 pp. DESIGNATED STATES: W: AM, AU, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, IS, JP, KG, KR, KZ, LK, LR, LT, LV, MD, MG, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TT, UA, UZ; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1995-US3948 19950331. PRIORITY: US 1994-222157 19940404.

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

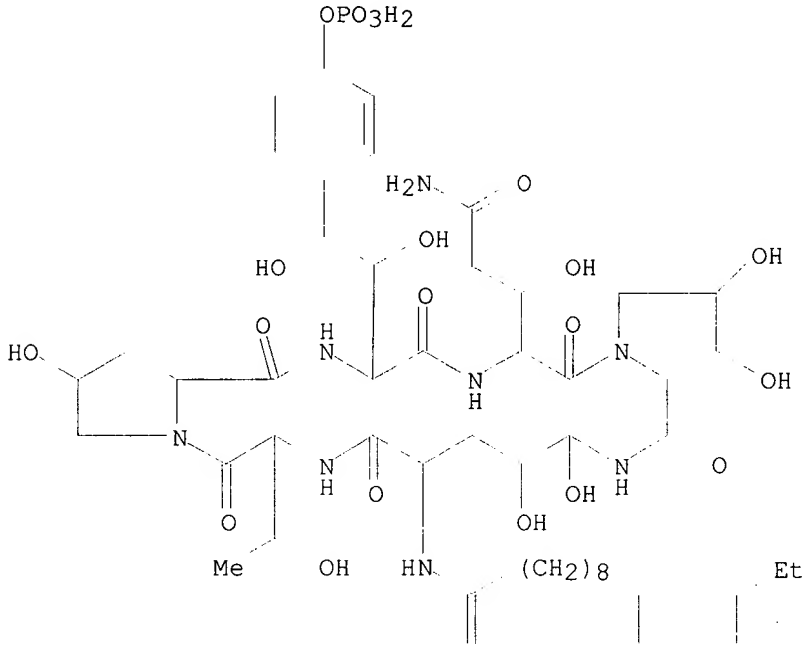
AB Title compds. [I; R = alkyl, alkenyl, Ph, biphenyl, naphthyl, terphenyl, alkylamino, dialkylamino, alkoxyaryl; R1, R2, R4 = H, OH; R3 = H, OH, O(CH2)nNRVRVI (RV, RVI, RVII = H, alkyl), O(CH2)nNRVRVIRVII+Y-; n = 2-6; Y = counterion; R5 = H, Me, OH; R6 = H, Me; R7 = H, Me, CH2C(:O)NH2, (CH2)2NRVRVI, (CH2)2NRVRVIRVII+Y-; R8 = Cl, Br, iodo, NO2, N3,

(CH2)0-4NH2, (CH2)0-4NHalkyl, (CH2)0-4N(alkyl)2, (CH2)0-3CH(:NOH), NHC(:O)(CH2)1-6NH2, NHC(:O)(CH2)1-6NHC(:NH)(CH2)0-3H], were prepd. Thus, title compd. (II) (prepd. from pneumocandin B0) showed a min. fungicidal concn. of 0.25 .mu.g/mL against Candida albicans MY1055.

L9 ANSWER 2 OF 14 REGISTRY COPYRIGHT 2000 ACS
RN 145680-60-0 REGISTRY
CN Pneumocandin A0, 6-[(2.alpha.,3.beta.,4.beta.)-3,4-dihydroxy-L-proline]-, 44-(dihydrogen phosphate) (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 1H-Dipyrrolo[2,1-c:2',1'-l][1,4,7,10,13,16]hexaazacycloheneicosine, cyclic
peptide deriv.
FS PROTEIN SEQUENCE
MF C50 H81 N8 O21 P
CI COM
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

Currently available stereo shown.

PAGE 1-A



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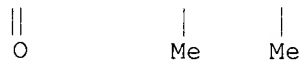

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 118:81447 Preparation of cyclic lipopeptides having antibiotic activity. Hammond, Milton L.; Balkovec, James M.; Mathre, David J. (Merck

and Co., Inc., USA). Eur. Pat. Appl. EP 503960 A1 19920916, 22 pp. DESIGNATED STATES: R: CH, DE, FR, GB, IT, LI, NL. (English). CODEN: EPXXDW. APPLICATION: EP 1992-302180 19920313. PRIORITY: US 1991-670604 19910315.

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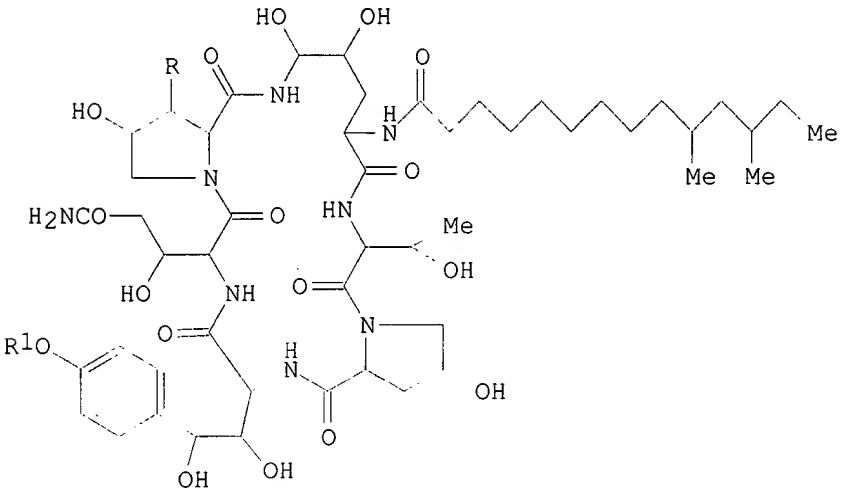


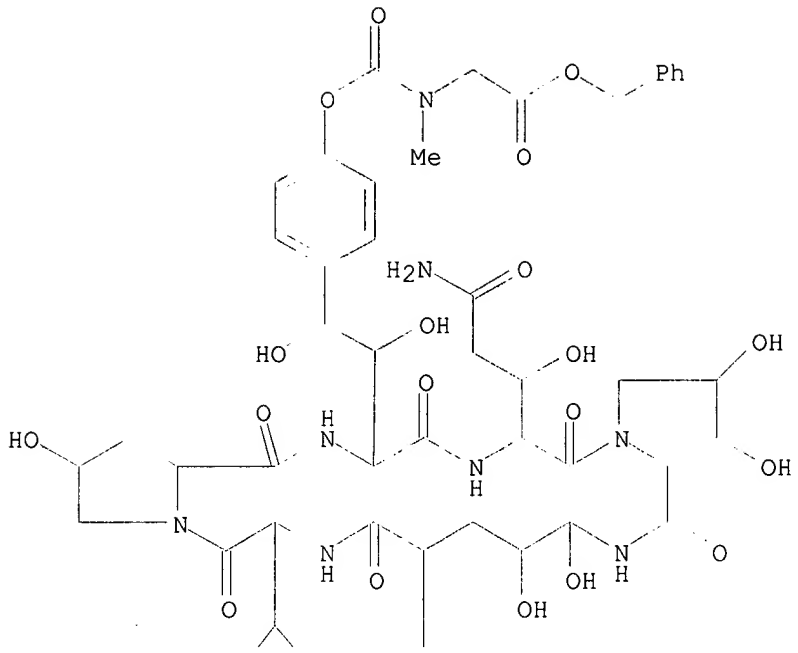
I

AB The prepn. of water-sol. derivs. of antibiotic lipopeptides I (R = H, OH; R1 = phosphono, sulfo, or acyl radical possessing a charged group at neutral pH is described. Thus, reaction of I (R = OH, R1 = H) (fermn. prepn. given) with tetrabenzyl pyrophosphate, followed by hydrogenolysis, gave I (R = OH, R1 = PO3H2) as its monopotassium salt. I have good soly. properties in aq. media, rendering them more useful as therapeutic agents against fungi (esp. Candida species), protozoa, and Pneumocystis carinii.

L9 ANSWER 3 OF 14 REGISTRY COPYRIGHT 2000 ACS
RN 145614-98-8 REGISTRY
CN Pneumocandin A0, 6-[(2.alpha.,3.beta.,4.beta.)-3,4-dihydroxy-L-proline]-, (44.fwdarw.N)-ester with N-carboxy-N-methylglycine 1-(phenylmethyl) ester (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 1H-Dipyrrolo[2,1-c:2',1'-l][1,4,7,10,13,16]hexaazacycloheneicosine, cyclic
peptide deriv.
FS PROTEIN SEQUENCE
MF C61 H91 N9 O21
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

Currently available stereo shown.

PAGE 1-A



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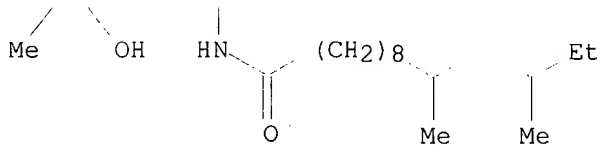

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 118:81447 Preparation of cyclic lipopeptides having antibiotic activity. Hammond, Milton L.; Balkovec, James M.; Mathre, David J. (Merck and Co., Inc., USA). Eur. Pat. Appl. EP 503960 A1 19920916, 22 pp. DESIGNATED STATES: R: CH, DE, FR, GB, IT, LI, NL. (English). CODEN: EPXXDW. APPLICATION: EP 1992-302180 19920313. PRIORITY: US 1991-670604 19910315.

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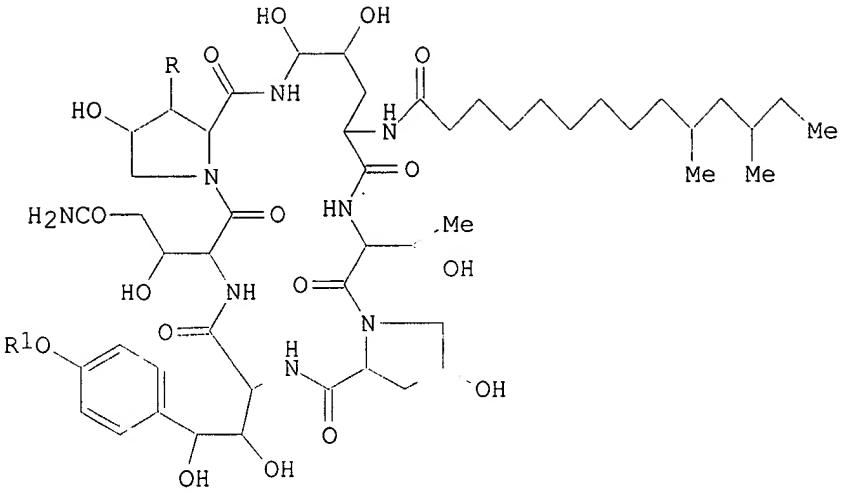


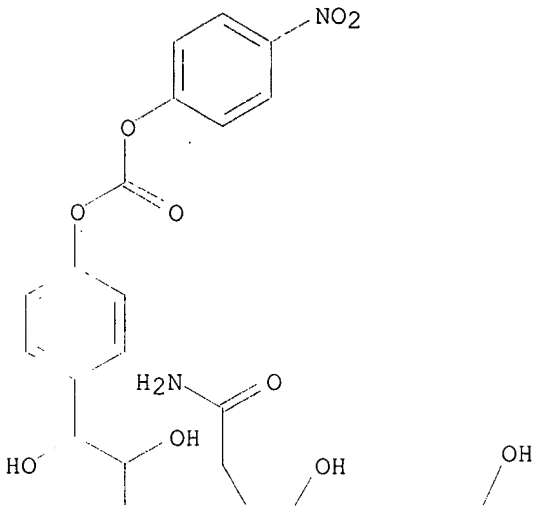
I

AB The prepn. of water-sol. derivs. of antibiotic lipopeptides I (R = H, OH; R1 = phosphono, sulfo, or acyl radical possessing a charged group at neutral pH is described. Thus, reaction of I (R = OH, R1 = H) (fermn. prepn. given) with tetrabenzyl pyrophosphate, followed by hydrogenolysis, gave I (R = OH, R1 = PO3H2) as its monopotassium salt. I have good soly. properties in aq. media, rendering them more useful as therapeutic agents against fungi (esp. Candida species), protozoa, and Pneumocystis carinii.

L9 ANSWER 4 OF 14 REGISTRY COPYRIGHT 2000 ACS
RN 145614-97-7 REGISTRY
CN Pneumocandin A0, 6-[(2.alpha.,3.beta.,4.beta.)-3,4-dihydroxy-L-proline]-, 44-(4-nitrophenyl carbonate) (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 1H-Dipyrrolo[2,1-c:2',1'-l][1,4,7,10,13,16]hexaazacycloheneicosine, cyclic
peptide deriv.
FS PROTEIN SEQUENCE
MF C57 H83 N9 O22
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

Currently available stereo shown.

PAGE 1-A



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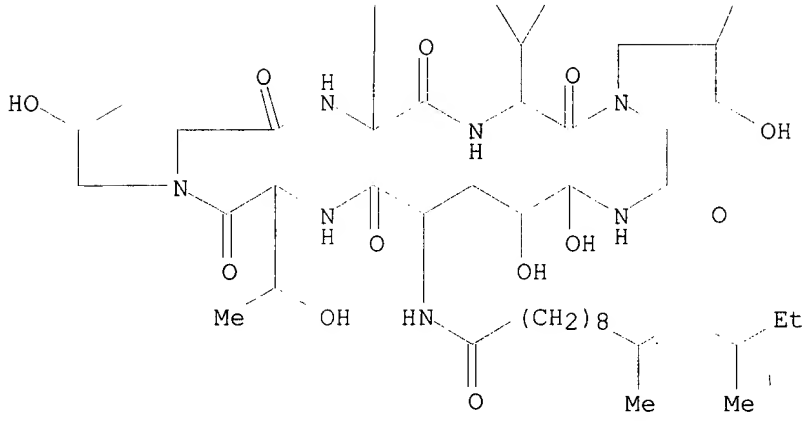
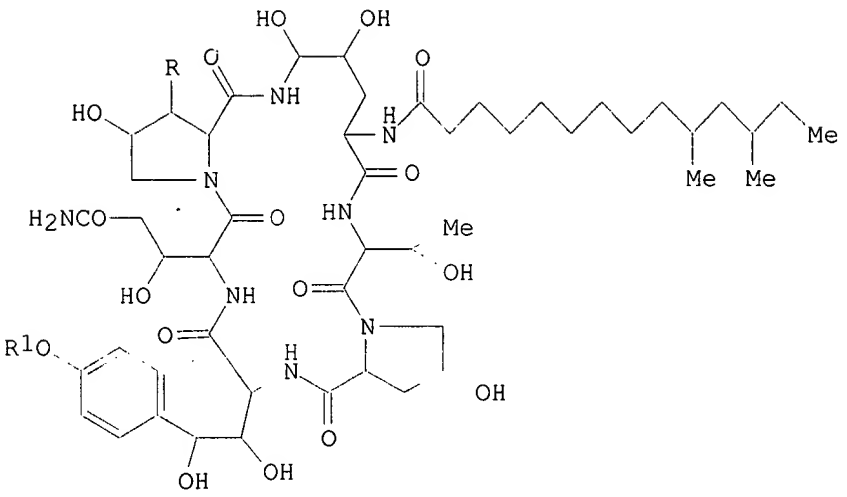


1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 118:81447 Preparation of cyclic lipopeptides having antibiotic activity. Hammond, Milton L.; Balkovec, James M.; Mathre, David J. (Merck and Co., Inc., USA). Eur. Pat. Appl. EP 503960 A1 19920916, 22 pp. DESIGNATED STATES: R: CH, DE, FR, GB, IT, LI, NL. (English). CODEN: EPXXDW. APPLICATION: EP 1992-302180 19920313. PRIORITY: US 1991-670604 19910315.

GI



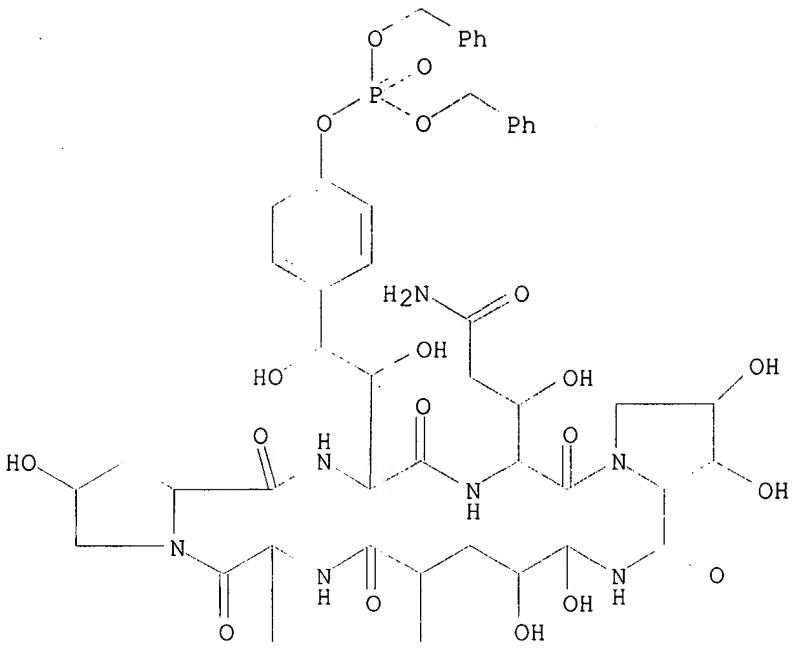
I

AB The prepn. of water-sol. derivs. of antibiotic lipopeptides I (R = H, OH; R1 = phosphono, sulfo, or acyl radical possessing a charged group at neutral pH is described. Thus, reaction of I (R = OH, R1 = H) (fermn. prepn. given) with tetrabenzyl pyrophosphate, followed by hydrogenolysis, gave I (R = OH, R1 = PO3H2) as its monopotassium salt. I have good soly. properties in aq. media, rendering them more useful as therapeutic agents against fungi (esp. Candida species), protozoa, and Pneumocystis carinii.

L9 ANSWER 5 OF 14 REGISTRY COPYRIGHT 2000 ACS
RN 145614-96-6 REGISTRY
CN Pneumocandin A0, 6-[(2.alpha.,3.beta.,4.beta.)-3,4-dihydroxy-L-proline]-, 44-[bis(phenylmethyl) phosphate] (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 1H-Dipyrrolo[2,1-c:2',1'-l][1,4,7,10,13,16]hexaazacycloheneicosine, cyclic
peptide deriv.
FS PROTEIN SEQUENCE
MF C64 H93 N8 O21 P
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

Currently available stereo shown.

PAGE 1-A



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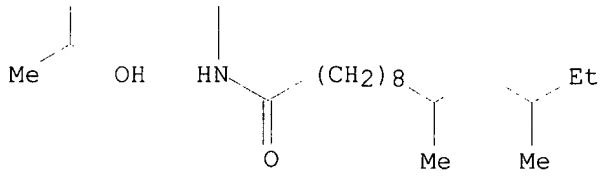
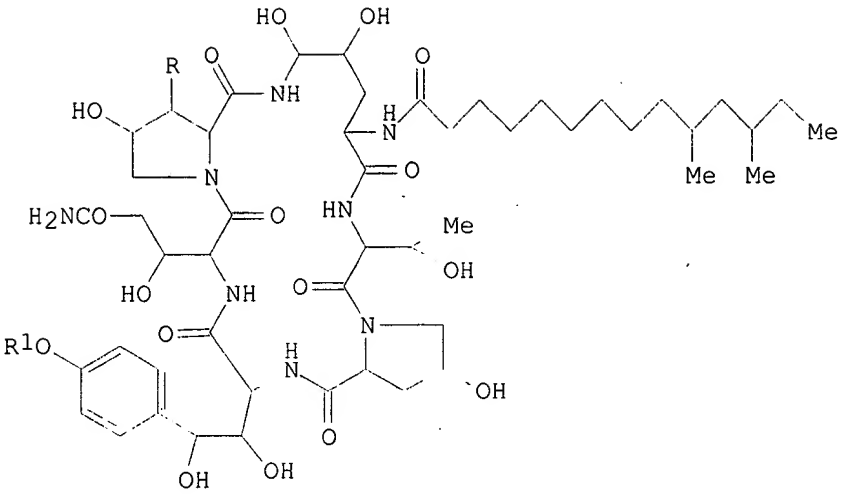


1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 118:81447 Preparation of cyclic lipopeptides having antibiotic activity. Hammond, Milton L.; Balkovec, James M.; Mathre, David J. (Merck and Co., Inc., USA). Eur. Pat. Appl. EP 503960 A1 19920916, 22 pp. DESIGNATED STATES: R: CH, DE, FR, GB, IT, LI, NL. (English). CODEN: EPXXDW. APPLICATION: EP 1992-302180 19920313. PRIORITY: US 1991-670604 19910315.

GI



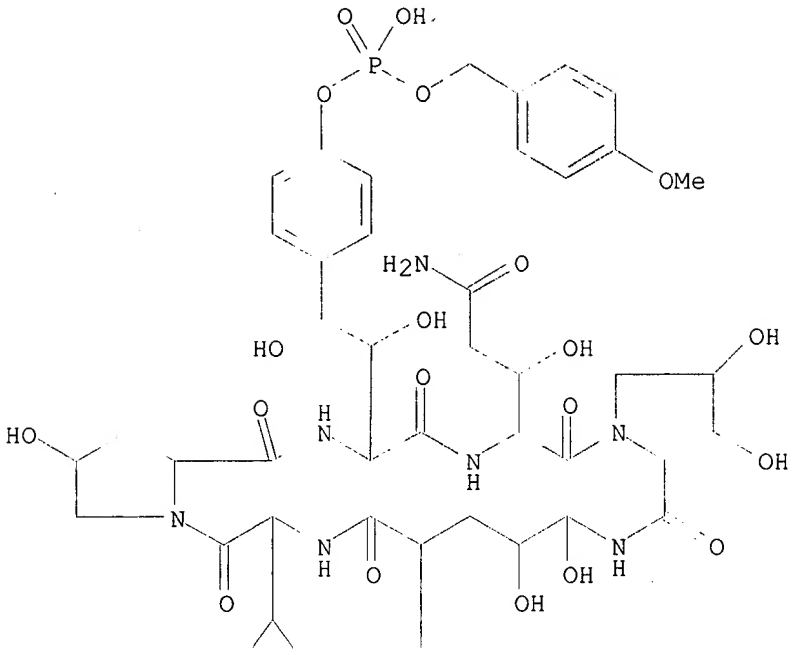
I

AB The prepn. of water-sol. derivs. of antibiotic lipopeptides I (R = H, OH; R1 = phosphono, sulfo, or acyl radical possessing a charged group at neutral pH is described. Thus, reaction of I (R = OH, R1 = H) (fermn. prepn. given) with tetrabenzyl pyrophosphate, followed by hydrogenolysis, gave I (R = OH, R1 = PO3H2) as its monopotassium salt. I have good soly. properties in aq. media, rendering them more useful as therapeutic agents against fungi (esp. Candida species), protozoa, and Pneumocystis carinii.

L9 ANSWER 6 OF 14 REGISTRY COPYRIGHT 2000 ACS
RN 145614-93-3 REGISTRY
CN Pneumocandin A0, 6-[(2.alpha.,3.beta.,4.beta.)-3,4-dihydroxy-L-proline]-, 44-[(4-methoxyphenyl)methyl hydrogen phosphate] (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 1H-Dipyrrolo[2,1-c:2',1'-l][1,4,7,10,13,16]hexaazacycloheneicosine, cyclic
peptide deriv.
FS PROTEIN SEQUENCE
MF C58 H89 N8 O22 P
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

Currently available stereo shown.

PAGE 1-A



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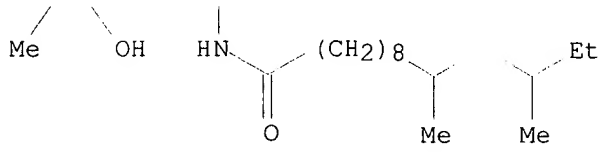

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 118:81447 Preparation of cyclic lipopeptides having antibiotic activity. Hammond, Milton L.; Balkovec, James M.; Mathre, David J. (Merck and Co., Inc., USA). Eur. Pat. Appl. EP 503960 A1 19920916, 22 pp. DESIGNATED STATES: R: CH, DE, FR, GB, IT, LI, NL. (English). CODEN: EPXXDW. APPLICATION: EP 1992-302180 19920313. PRIORITY: US 1991-670604 19910315.

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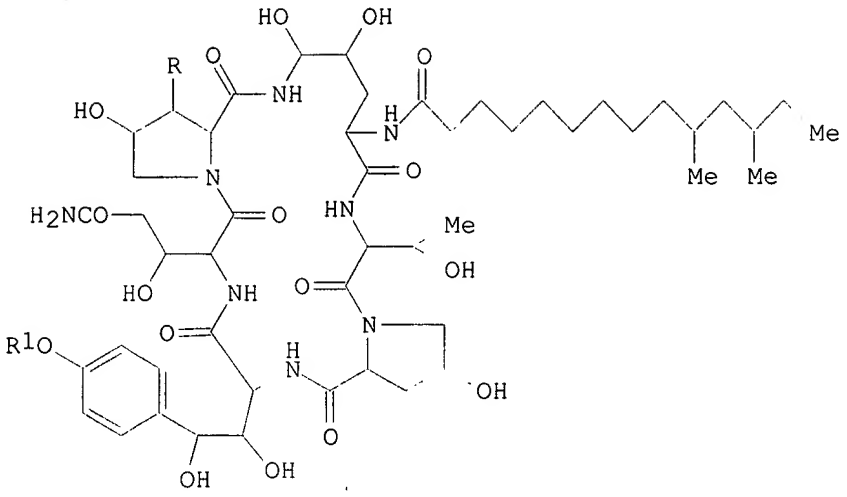


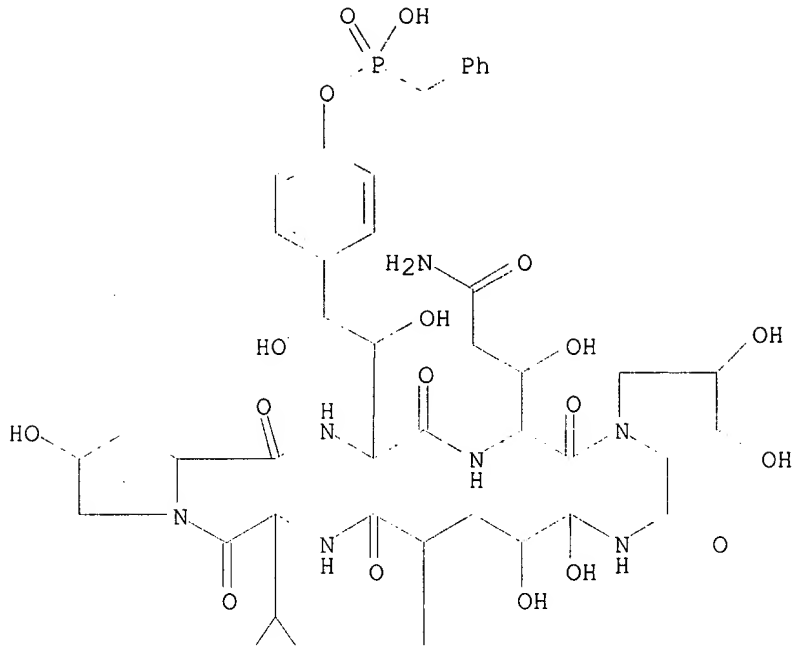
I

AB The prepn. of water-sol. derivs. of antibiotic lipopeptides I (R = H, OH; R1 = phosphono, sulfo, or acyl radical possessing a charged group at neutral pH is described. Thus, reaction of I (R = OH, R1 = H) (fermn. prepn. given) with tetrabenzyl pyrophosphate, followed by hydrogenolysis, gave I (R = OH, R1 = PO3H2) as its monopotassium salt. I have good soly. properties in aq. media, rendering them more useful as therapeutic agents against fungi (esp. Candida species), protozoa, and Pneumocystis carinii.

L9 ANSWER 7 OF 14 REGISTRY COPYRIGHT 2000 ACS
RN 145614-92-2 REGISTRY
CN Pneumocandin A0, 6-[(2.alpha.,3.beta.,4.beta.)-3,4-dihydroxy-L-proline]-, 44-[hydrogen (phenylmethyl)phosphonate] (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 1H-Dipyrrolo[2,1-c:2',1'-l][1,4,7,10,13,16]hexaazacycloheneicosine, cyclic
peptide deriv.
FS PROTEIN SEQUENCE
MF C57 H87 N8 O20 P
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

Currently available stereo shown.

PAGE 1-A



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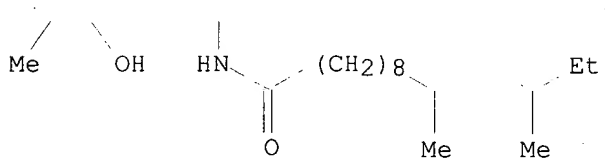

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 118:81447 Preparation of cyclic lipopeptides having antibiotic activity. Hammond, Milton L.; Balkovec, James M.; Mathre, David J. (Merck and Co., Inc., USA). Eur. Pat. Appl. EP 503960 A1 19920916, 22 pp. DESIGNATED STATES: R: CH, DE, FR, GB, IT, LI, NL. (English). CODEN: EPXXDW. APPLICATION: EP 1992-302180 19920313. PRIORITY: US 1991-670604 19910315.

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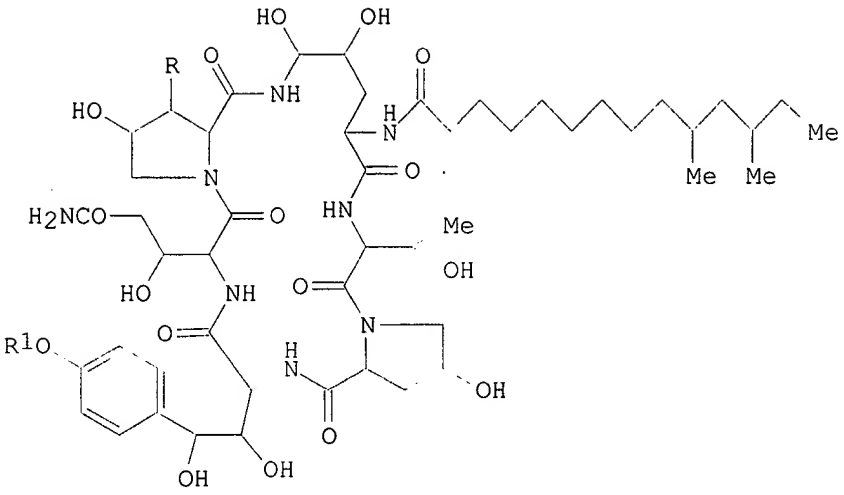

I

AB The prepn. of water-sol. derivs. of antibiotic lipopeptides I (R = H, OH; R1 = phosphono, sulfo, or acyl radical possessing a charged group at neutral pH is described. Thus, reaction of I (R = OH, R1 = H) (fermn. prepn. given) with tetrabenzyl pyrophosphate, followed by hydrogenolysis, gave I (R = OH, R1 = PO3H2) as its monopotassium salt. I have good soly. properties in aq. media, rendering them more useful as therapeutic agents against fungi (esp. Candida species), protozoa, and Pneumocystis carinii.

L9 ANSWER 8 OF 14 REGISTRY COPYRIGHT 2000 ACS
RN 145614-91-1 REGISTRY
CN Pneumocandin A0, 6-[(2.alpha.,3.beta.,4.beta.)-3,4-dihydroxy-L-proline]-, 44-(ethyl hydrogen phosphate) (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 1H-Dipyrrolo[2,1-c:2',1'-l][1,4,7,10,13,16]hexaazacycloheneicosine, cyclic
peptide deriv.
FS PROTEIN SEQUENCE
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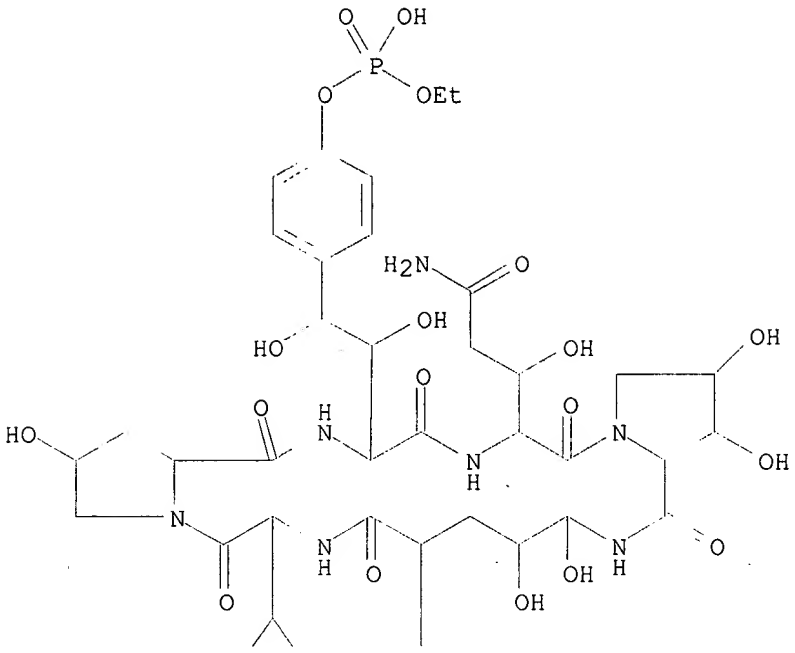
LC STN Files: CA, CAPLUS, USPATFULL

Currently available stereo shown.

PAGE 1-A



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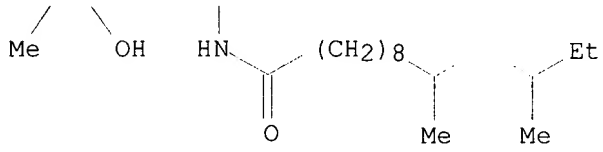
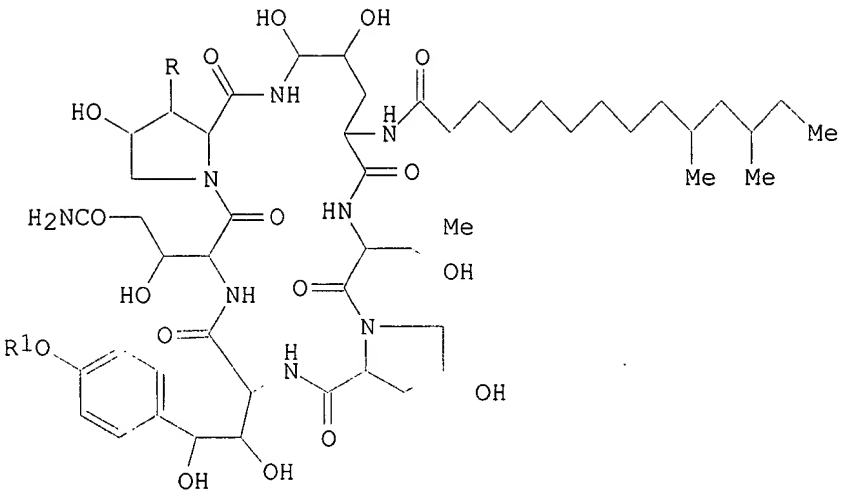


1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 118:81447 Preparation of cyclic lipopeptides having antibiotic activity. Hammond, Milton L.; Balkovec, James M.; Mathre, David J. (Merck and Co., Inc., USA). Eur. Pat. Appl. EP 503960 A1 19920916, 22 pp. DESIGNATED STATES: R: CH, DE, FR, GB, IT, LI, NL. (English). CODEN: EPXXDW. APPLICATION: EP 1992-302180 19920313. PRIORITY: US 1991-670604 19910315.

GI



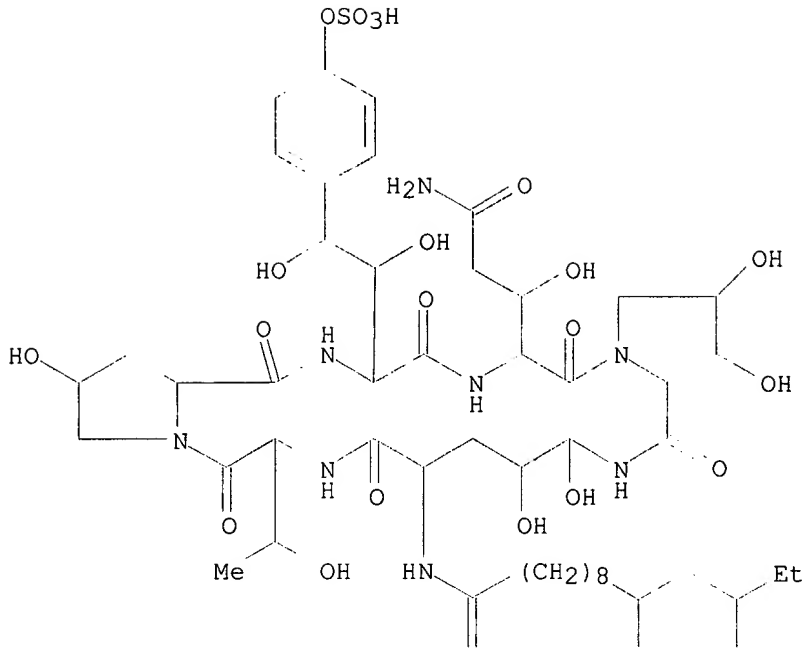
I

AB The prepn. of water-sol. derivs. of antibiotic lipopeptides I (R = H, OH; R1 = phosphono, sulfo, or acyl radical possessing a charged group at neutral pH is described. Thus, reaction of I (R = OH, R1 = H) (fermn. prepn. given) with tetrabenzyl pyrophosphate, followed by hydrogenolysis, gave I (R = OH, R1 = PO3H2) as its monopotassium salt. I have good soly. properties in aq. media, rendering them more useful as therapeutic agents against fungi (esp. Candida species), protozoa, and Pneumocystis carinii.

L9 ANSWER 9 OF 14 REGISTRY COPYRIGHT 2000 ACS
RN 145614-85-3 REGISTRY
CN Pneumocandin A0, 6-[(2.alpha.,3.beta.,4.beta.)-3,4-dihydroxy-L-proline]-, 44-(hydrogen sulfate) (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 1H-Dipyrrolo[2,1-c:2',1'-l][1,4,7,10,13,16]hexaazacycloheneicosine, cyclic
peptide deriv.
FS PROTEIN SEQUENCE
MF C50 H80 N8 O21 S
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

Currently available stereo shown.

PAGE 1-A



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1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 118:81447 Preparation of cyclic lipopeptides having antibiotic activity. Hammond, Milton L.; Balkovec, James M.; Mathre, David J. (Merck and Co., Inc., USA). Eur. Pat. Appl. EP 503960 A1 19920916, 22 pp. DESIGNATED STATES: R: CH, DE, FR, GB, IT, LI, NL. (English). CODEN: EPXXDW. APPLICATION: EP 1992-302180 19920313. PRIORITY: US 1991-670604 19910315.

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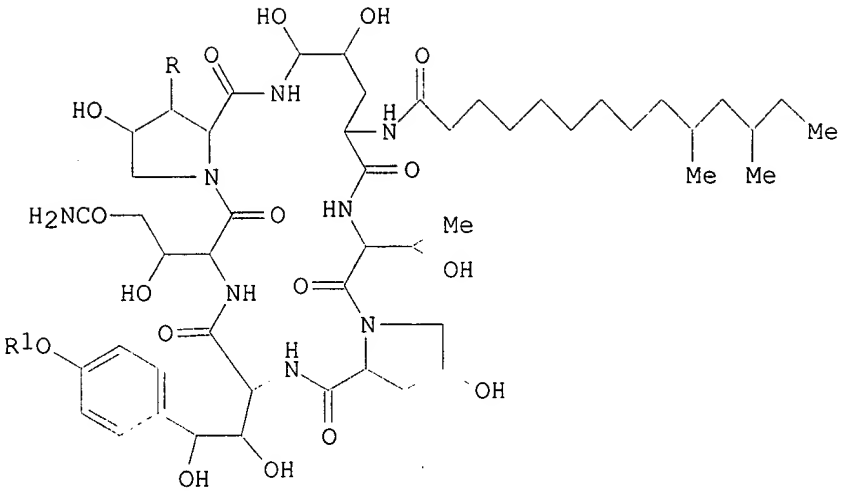


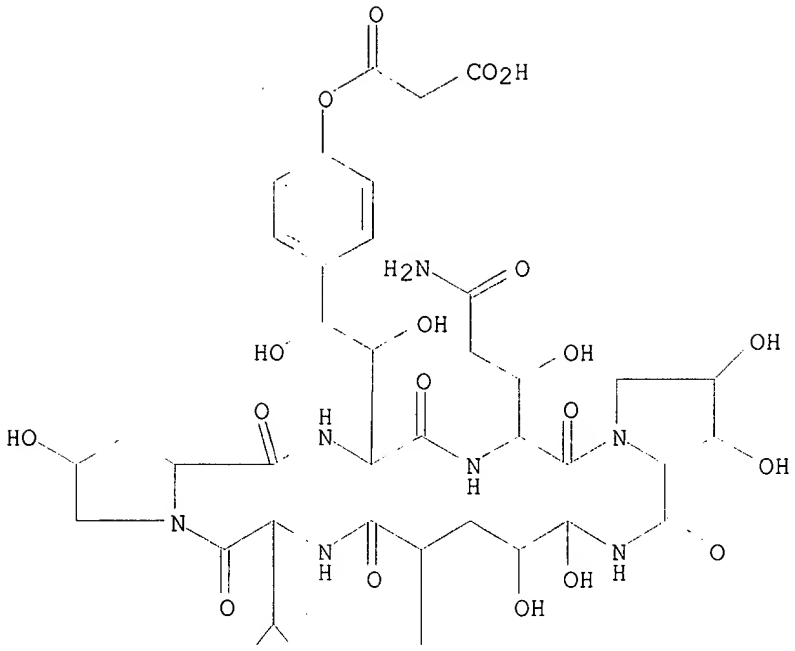
I

AB The prepn. of water-sol. derivs. of antibiotic lipopeptides I (R = H, OH; R1 = phosphono, sulfo, or acyl radical possessing a charged group at neutral pH is described. Thus, reaction of I (R = OH, R1 = H) (fermn. prepn. given) with tetrabenzyl pyrophosphate, followed by hydrogenolysis, gave I (R = OH, R1 = PO3H2) as its monopotassium salt. I have good soly. properties in aq. media, rendering them more useful as therapeutic agents against fungi (esp. Candida species), protozoa, and Pneumocystis carinii.

L9 ANSWER 10 OF 14 REGISTRY COPYRIGHT 2000 ACS
RN 145614-84-2 REGISTRY
CN Pneumocandin A0, 6-[(2.alpha.,3.beta.,4.beta.)-3,4-dihydroxy-L-proline]-, 44-(hydrogen propanedioate) (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 1H-Dipyrrolo[2,1-c:2',1'-l][1,4,7,10,13,16]hexaazacycloheneicosine, cyclic
peptide deriv.
FS PROTEIN SEQUENCE
MF C53 H82 N8 O21
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

Currently available stereo shown.

PAGE 1-A



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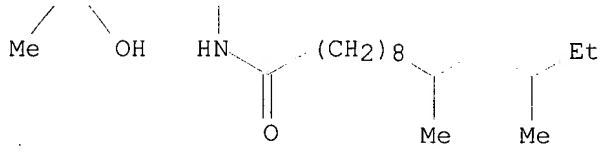

1 REFERENCES IN FILE CA (1967 TO DATE)
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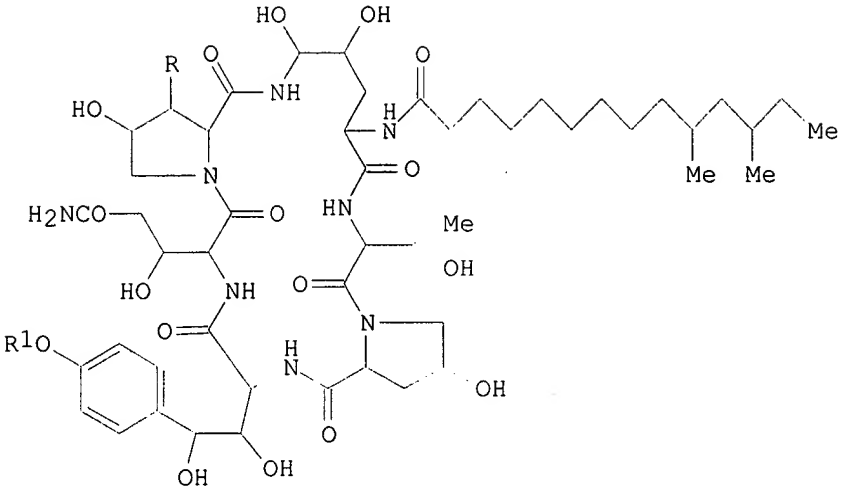
REFERENCE 1: 118:81447 Preparation of cyclic lipopeptides having antibiotic activity. Hammond, Milton L.; Balkovec, James M.; Mathre, David J. (Merck and Co., Inc., USA). Eur. Pat. Appl. EP 503960 A1 19920916, 22 pp. DESIGNATED STATES: R: CH, DE, FR, GB, IT, LI, NL. (English). CODEN: EPXXDW. APPLICATION: EP 1992-302180 19920313. PRIORITY: US 1991-670604 19910315.

GI



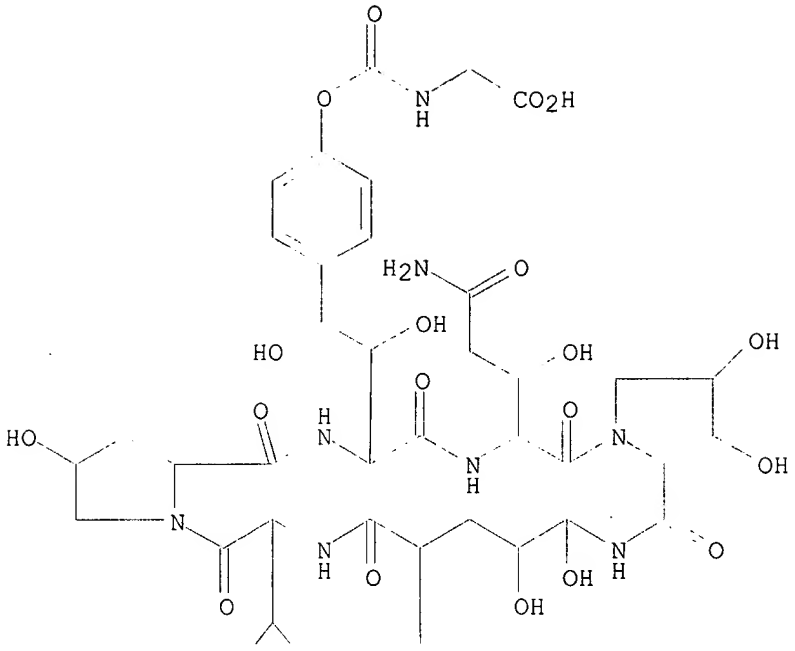
I

AB The prepn. of water-sol. derivs. of antibiotic lipopeptides I (R = H, OH; R1 = phosphono, sulfo, or acyl radical possessing a charged group at neutral pH is described. Thus, reaction of I (R = OH, R1 = H) (fermn. prepn. given) with tetrabenzyl pyrophosphate, followed by hydrogenolysis, gave I (R = OH, R1 = PO3H2) as its monopotassium salt. I have good soly. properties in aq. media, rendering them more useful as therapeutic agents against fungi (esp. Candida species), protozoa, and Pneumocystis carinii.

L9 ANSWER 11 OF 14 REGISTRY COPYRIGHT 2000 ACS
RN 145614-82-0 REGISTRY
CN Pneumocandin A0, 6-[(2.alpha.,3.beta.,4.beta.)-3,4-dihydroxy-L-proline]-, (44.fwdarw.N)-ester with N-carboxyglycine (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 1H-Dipyrrolo[2,1-c:2',1'-l][1,4,7,10,13,16]hexaazacycloheneicosine, cyclic
peptide deriv.
FS PROTEIN SEQUENCE
MF C53 H83 N9 O21
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

Currently available stereo shown.

PAGE 1-A



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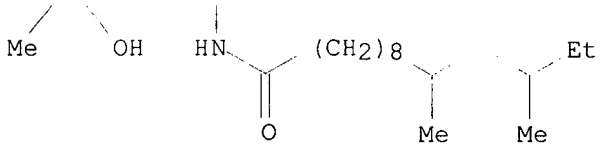

1 REFERENCES IN FILE CA (1967 TO DATE)
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REFERENCE 1: 118:81447 Preparation of cyclic lipopeptides having antibiotic activity. Hammond, Milton L.; Balkovec, James M.; Mathre, David J. (Merck and Co., Inc., USA). Eur. Pat. Appl. EP 503960 A1 19920916, 22 pp. DESIGNATED STATES: R: CH, DE, FR, GB, IT, LI, NL. (English). CODEN: EPXXDW. APPLICATION: EP 1992-302180 19920313. PRIORITY: US 1991-670604 19910315.

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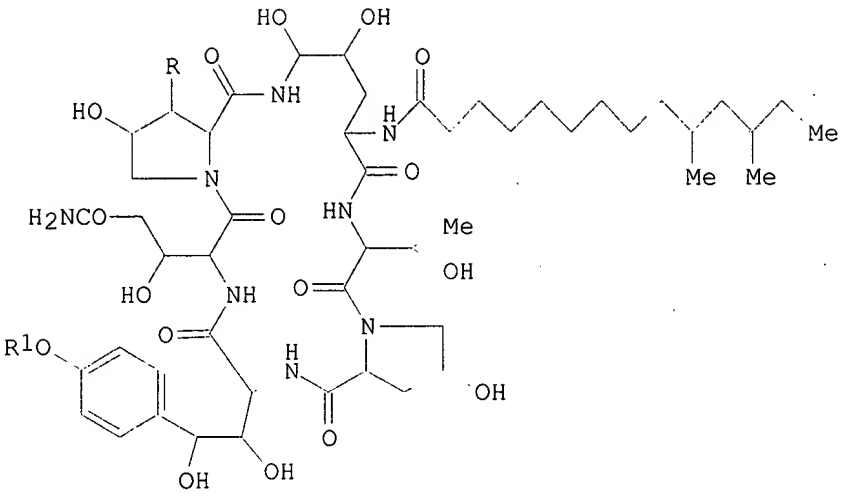


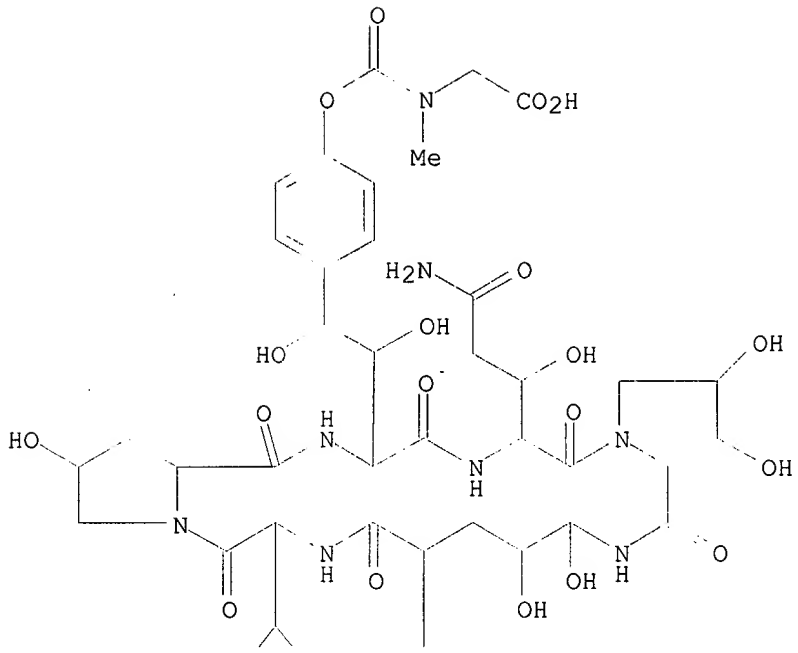
I

AB The prepn. of water-sol. derivs. of antibiotic lipopeptides I (R = H, OH; R1 = phosphono, sulfo, or acyl radical possessing a charged group at neutral pH is described. Thus, reaction of I (R = OH, R1 = H) (fermn. prepn. given) with tetrabenzyl pyrophosphate, followed by hydrogenolysis, gave I (R = OH, R1 = PO3H2) as its monopotassium salt. I have good soly. properties in aq. media, rendering them more useful as therapeutic agents against fungi (esp. Candida species), protozoa, and Pneumocystis carinii.

L9 ANSWER 12 OF 14 REGISTRY COPYRIGHT 2000 ACS
RN 145614-81-9 REGISTRY
CN Pneumocandin A0, 6-[(2.alpha.,3.beta.,4.beta.)-3,4-dihydroxy-L-proline]-, (44.fwdarw.N)-ester with N-carboxy-N-methylglycine (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 1H-Dipyrrolo[2,1-c:2',1'-l][1,4,7,10,13,16]hexaazacycloheneicosine, cyclic
peptide deriv.
FS PROTEIN SEQUENCE
MF C54 H85 N9 O21
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

Currently available stereo shown.

PAGE 1-A



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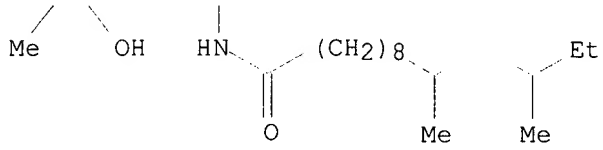

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 118:81447 Preparation of cyclic lipopeptides having antibiotic activity. Hammond, Milton L.; Balkovec, James M.; Mathre, David J. (Merck and Co., Inc., USA). Eur. Pat. Appl. EP 503960 A1 19920916, 22 pp. DESIGNATED STATES: R: CH, DE, FR, GB, IT, LI, NL. (English). CODEN: EPXXDW. APPLICATION: EP 1992-302180 19920313. PRIORITY: US 1991-670604 19910315.

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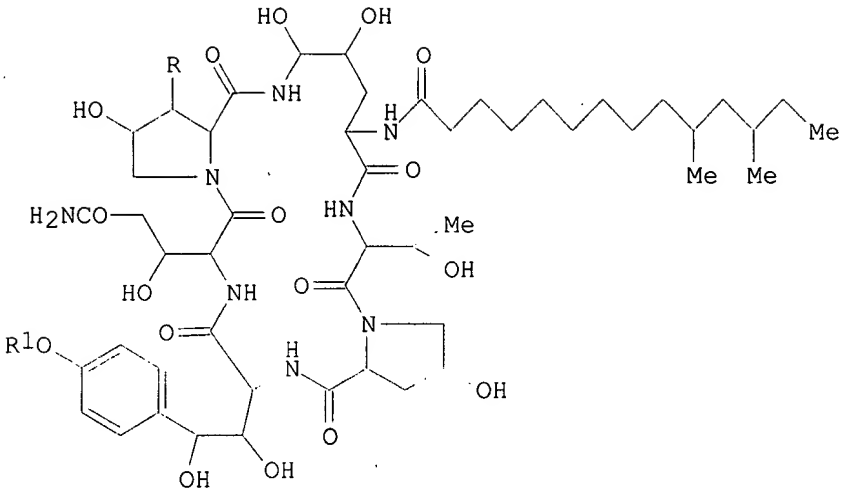
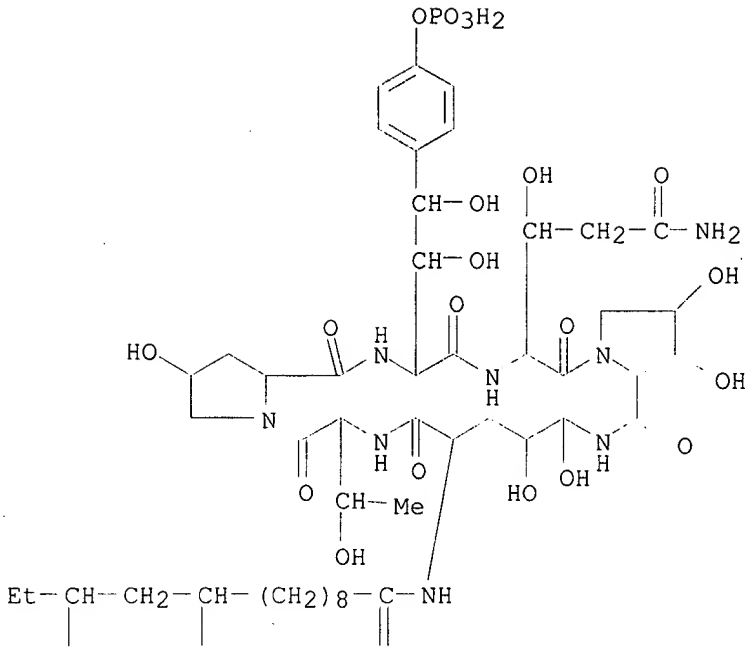


I

AB The prepn. of water-sol. derivs. of antibiotic lipopeptides I (R = H, OH; R1 = phosphono, sulfo, or acyl radical possessing a charged group at neutral pH is described. Thus, reaction of I (R = OH, R1 = H) (fermn. prepn. given) with tetrabenzyl pyrophosphate, followed by hydrogenolysis, gave I (R = OH, R1 = PO3H2) as its monopotassium salt. I have good soly. properties in aq. media, rendering them more useful as therapeutic agents against fungi (esp. Candida species), protozoa, and Pneumocystis carinii.

L9 ANSWER 13 OF 14 REGISTRY COPYRIGHT 2000 ACS
RN 145614-80-8 REGISTRY
CN Pneumocandin A0, 6-[(2.alpha.,3.beta.,4.beta.)-3,4-dihydroxy-L-proline]-, 44-(dihydrogen phosphate), monopotassium salt (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 1H-Dipyrrolo[2,1-c:2',1'-l][1,4,7,10,13,16]hexaazacycloheneicosine, cyclic
peptide deriv.
FS PROTEIN SEQUENCE
MF C50 H81 N8 O21 P . K
SR CA
LC STN Files: CA, CAPLUS, USPATFULL
CRN (145680-60-0)

PAGE 1-A



PAGE 2-A

K

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 118:81447 Preparation of cyclic lipopeptides having antibiotic activity. Hammond, Milton L.; Balkovec, James M.; Mathre, David J. (Merck and Co., Inc., USA). Eur. Pat. Appl. EP 503960 A1 19920916, 22 pp. DESIGNATED STATES: R: CH, DE, FR, GB, IT, LI, NL. (English). CODEN: EPXXDW. APPLICATION: EP 1992-302180 19920313. PRIORITY: US 1991-670604 19910315.

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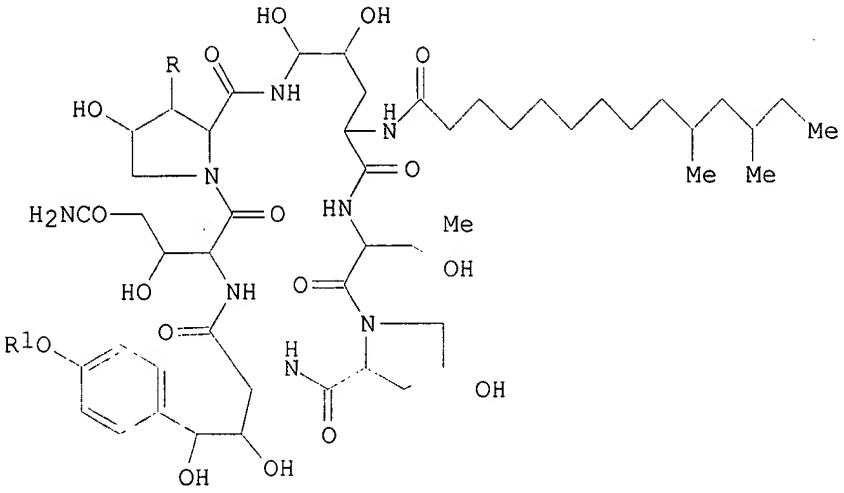


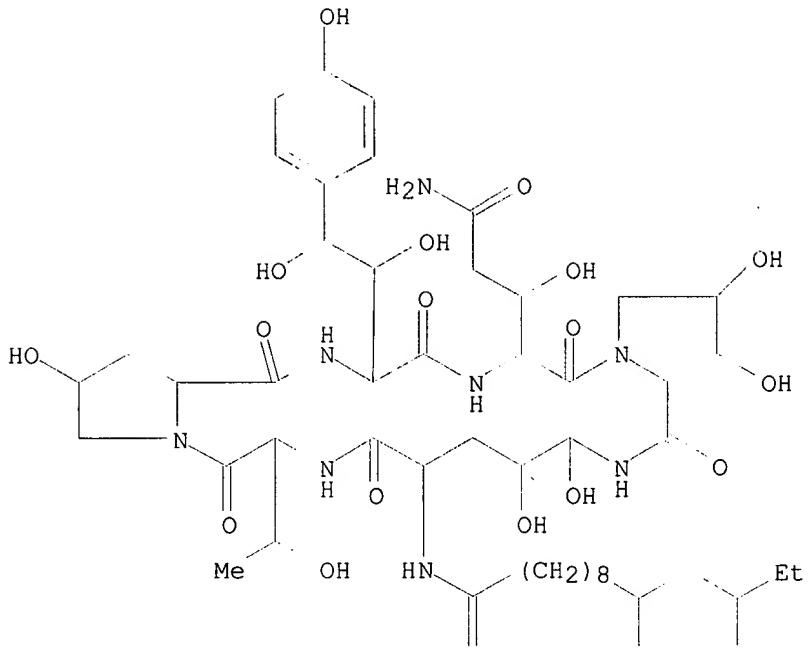
I

AB The prepn. of water-sol. derivs. of antibiotic lipopeptides I (R = H, OH; R1 = phosphono, sulfo, or acyl radical possessing a charged group at neutral pH is described. Thus, reaction of I (R = OH, R1 = H) (fermn. prepn. given) with tetrabenzyl pyrophosphate, followed by hydrogenolysis, gave I (R = OH, R1 = PO3H2) as its monopotassium salt. I have good soly. properties in aq. media, rendering them more useful as therapeutic agents against fungi (esp. Candida species), protozoa, and Pneumocystis carinii.

L9 ANSWER 14 OF 14 REGISTRY COPYRIGHT 2000 ACS
RN 144087-99-0 REGISTRY
CN Pneumocandin D0 (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 1H-Dipyrrolo[2,1-c:2',1'-l][1,4,7,10,13,16]hexaazacycloheneicosine, cyclic
peptide deriv.
CN Pneumocandin B0, 6-[(2.alpha.,3.beta.,4.beta.)-3,4-dihydroxy-L-proline]-
OTHER NAMES:
CN Pneumocandin D0 (Zalerion arboricola)
FS PROTEIN SEQUENCE
DR 145680-58-6, 157536-07-7
MF C50 H80 N8 O18
SR CA
LC STN Files: CA, CAPLUS, DRUGUPDATES, MEDLINE, USPATFULL

Currently available stereo shown.

PAGE 1-A



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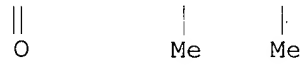
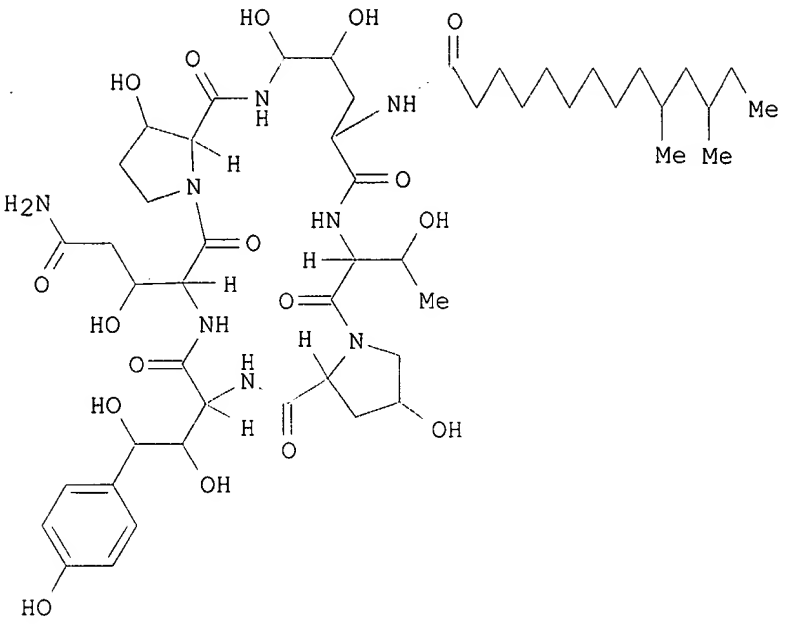


5 REFERENCES IN FILE CA (1967 TO DATE)
5 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 132:165211 Method for the production of an antibiotic agent. Connors, Neal C.; Petersen, Leslie A.; Hughes, David L.; Dimichele, Lisa M.; Novak, Thomas J. (Merck & Co., Inc., USA). PCT Int. Appl. WO 2000008197 A1 20000217, 18 pp. DESIGNATED STATES: W: AE, AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CR, CU, CZ, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TM, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1999-US17444 19990804. PRIORITY: US 1998-95691 19980807.

GI



I

AB An improved process for prepg. the compd. of formula (I) is disclosed which utilizes certain amino acids and divalent cations such as Ni, Co, and Zn to increase titer and decrease the amt. of structural analogs.

REFERENCE 2: 131:71075 Reclassification of a pneumocandin-producing anamorph, Glarea lozoyensis gen. et sp. nov., previously identified as Zalerion arboricola. Bills, Gerald F.; Platas, Gonzalo; Pelaez, Fernando;
Masurekar, Prakash (Natural Products Drug Discovery, Merck Research Laboratories, Rahway, NJ, 07065-0900, USA). Mycol. Res., 103(2), 179-192 (English) 1999. CODEN: MYCRER. ISSN: 0953-7562. Publisher: Cambridge University Press.

AB The importance of pneumocandin B0 as the fermn.-derived starting material for the antifungal drug candidate, MK-991, along with the identification of the prodn. strain as Z. arboricola (ATCC 20868) as CBS prompted a search for other strains of Z. arboricola or Zalerion species with improved titers or that might produce natural pneumocandin analogs. Anal.
of morphol., secondary metabolites profiles, and DNA fingerprinting demonstrated that ATCC 20868 was not congeneric with Z. arboricola. Ribosomal DNA sequences were compared among Zalerion species and pneumocandin-producing fungi and with rDNA sequences in GenBank. No good matches with sequences in GenBank were obtained for Z. arboricola or Z. maritimum, but for Z. varium, P. carpinea and ATCC 20868, relevant similarities were obsd. with ITS1 sequences from fungi of Leotiales. ATCC
20868 was phylogenetically more akin to P. carpinea, another pneumocandin producer, than initially suspected. The closest relative of ATCC 20868 seemed to be Hymenoscyphus monotropae. Thus, it is concluded that the genus Zelerion is artificial; its species bear no phylogenetic relation among themselves. ATCC 20868 and Z. varium were related to fungi of the Leotiales. A new anamorph genus and species, Glarea lozoyensis, is proposed to accommodate ATCC 20868.

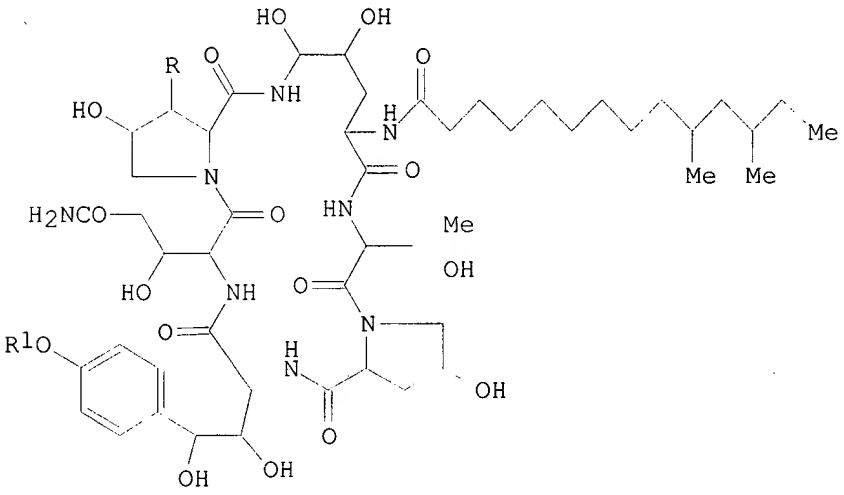
REFERENCE 3: 122:79204 Antibiotic agent. Schwartz, Robert E.; Masurekar,

Prakash S.; Sesin, David F.; Liesch, Jerrold M.; Hallada, Thomas C.; Hensens, Otto D. (Merck and Co., Inc., USA). U.S. US 5366880 A 19941122,
13 pp. Division of U.S. Ser. No.640,457. (English). CODEN: USXXAM. APPLICATION: US 1993-66282 19930521. PRIORITY: US 1990-640457 19901219.

AB A new antibiotic cyclic lipopeptide and a method of its prodn. by cultivation of a mutant of Zalerion arboricola is described. The agent has very high activity against human pathogens and is of very low mammalian toxicity.

REFERENCE 4: 118:81447 Preparation of cyclic lipopeptides having antibiotic activity. Hammond, Milton L.; Balkovec, James M.; Mathre, David J. (Merck
and Co., Inc., USA). Eur. Pat. Appl. EP 503960 A1 19920916, 22 pp. DESIGNATED STATES: R: CH, DE, FR, GB, IT, LI, NL. (English). CODEN: EPXXDW. APPLICATION: EP 1992-302180 19920313. PRIORITY: US 1991-670604 19910315.

GI



I

AB The prepn. of water-sol. derivs. of antibiotic lipopeptides I (R = H, OH; R1 = phosphono, sulfo, or acyl radical possessing a charged group at neutral pH is described. Thus, reaction of I (R = OH, R1 = H) (fermn. prepn. given) with tetrabenzyl pyrophosphate, followed by hydrogenolysis, gave I (R = OH, R1 = PO3H2) as its monopotassium salt. I have good soly. properties in aq. media, rendering them more useful as therapeutic agents against fungi (esp. Candida species), protozoa, and Pneumocystis carinii.

REFERENCE 5: 117:190270 Cyclic lipopeptide antibiotics and their manufacture
with Zalerion arboricola. Schwartz, Robert E.; Hallada, Thomas C.; Masurekar, Prakash S.; Hensens, Otto D.; Liesch, Jerrold M.; Sesin, David F. (Merck and Co., Inc., USA). Eur. Pat. Appl. EP 494515 A1 19920715, 21 pp. DESIGNATED STATES: R: AT, BE, CH, DE, DK, ES, FR, GB, IT, LI, LU, NL, SE. (English). CODEN: EPXXDW. APPLICATION: EP 1991-311530 19911211.
PRIORITY: US 1990-630457 19901219.

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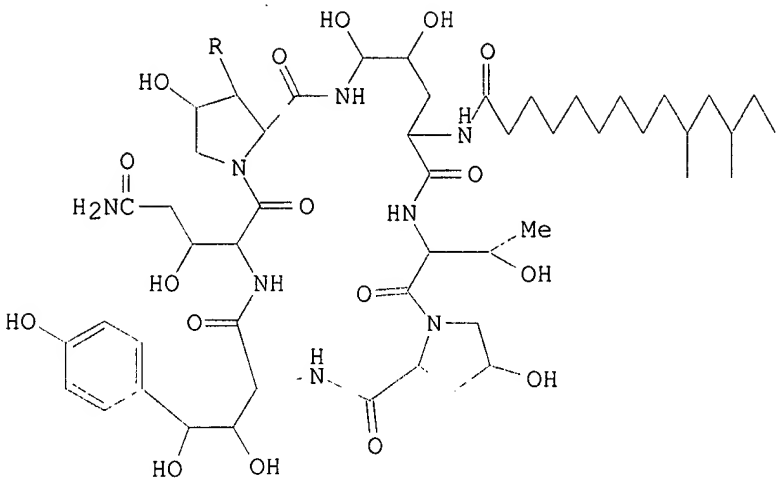

I

AB Cyclic lipopeptide antibiotics I (R=H,OH) are isolated from Z. arboricola mutant fermn. broth. The activity of these compds. against Candida and Pneumocystis carinii was demonstrated.

```
=> s ?boronic acid?/cns

          6044 ?BORONIC/CNS
       4634268 ACID?/CNS
L10       6002 ?BORONIC ACID?/CNS
                 ((?BORONIC(W)ACID?)/CNS)

=> s ?boric acid?/cns

          5391 ?BORIC/CNS
       4634268 ACID?/CNS
L11       5385 ?BORIC ACID?/CNS
                 ((?BORIC(W)ACID?)/CNS)

=> s cyclic peptide

         75134 CYCLIC
         45965 PEPTIDE
           461 PEPTIDES
         45965 PEPTIDE
                 (PEPTIDE OR PEPTIDES)
L12      23113 CYCLIC PEPTIDE
                 (CYCLIC(W)PEPTIDE)

=> s cyclo peptide

       2486823 CYCLO
            11 CYCLOS
       2486823 CYCLO
                 (CYCLO OR CYCLOS)
         45965 PEPTIDE
           461 PEPTIDES
         45965 PEPTIDE
                 (PEPTIDE OR PEPTIDES)
```

L13 15 CYCLO PEPTIDE
(CYCLO(W)PEPTIDE)

=> fil medl,caplus,biosis,embase,wpids;s (l10 or l11 or ?boronic acid? or ?boric acid?) and (l12 or l13 or (cyclo or cyclic)(w)peptide)

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FULL ESTIMATED COST	459.66	729.28

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CA SUBSCRIBER PRICE	-7.42	-9.09

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There are limits on the size of an answer set being crossed over from one file to another. Enter HELP CROSSOVER at an arrow prompt (=>) for specific information.

=> fil reg

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	5.04	734.32

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	0.00	-9.09

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```
=> s l12 or l12

L14      23113 L12 OR L12

=> d 9000 18000 reg

9000      RN             128481-41-4  REGISTRY
18000     RN              78806-26-5  REGISTRY


=> s l14 range=(128481-41-4,)

L15       9000 L12 OR L12

=> s l14 range=(78806-26-5,128481-41-4)

L16       9001 L12 OR L12

=> s l14 range=(,78806-26-5)

L17       5114 L12 OR L12

=> fil medl,caplus,biosis,embase,wpids

COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                         ENTRY    SESSION
FULL ESTIMATED COST                                       0.60     734.92

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
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=> s (l10 or l11 or ?boronic acid? or ?boric acid?) and (l15 or l16 or l17 or
l13 or (cyclo or cyclic)(w)peptide)

L18          6 FILE MEDLINE
L19         74 FILE CAPLUS
L20          8 FILE BIOSIS
L21         19 FILE EMBASE
LEFT TRUNCATION IGNORED FOR '?BORONIC' FOR FILE 'WPIDS'
LEFT TRUNCATION IGNORED FOR '?BORIC' FOR FILE 'WPIDS'
L22          3 FILE WPIDS

TOTAL FOR ALL FILES
```

L23 110 (L10 OR L11 OR ?BORONIC ACID? OR ?BORIC ACID?) AND (L15 OR L16 OR L17 OR L13 OR (CYCLO OR CYCLIC)(W) PEPTIDE)
Left truncation is not valid in the specified search field in the specified file. The term has been searched without left truncation. Examples: '?TERPEN?' would be searched as 'TERPEN?' and '?FLAVONOID' would be searched as 'FLAVONOID.'

If you are searching in a field that uses implied proximity, and you used a truncation symbol after a punctuation mark, the system may interpret the truncation symbol as being at the beginning of a term. Implied proximity is used in search fields indexed as single words, for example, the Basic Index.

=> s l23 and (purif? or revers?)

L24 1 FILE MEDLINE
L25 14 FILE CAPLUS
L26 0 FILE BIOSIS
L27 0 FILE EMBASE
L28 1 FILE WPIDS

TOTAL FOR ALL FILES
L29 16 L23 AND (PURIF? OR REVERS?)

=> s l29 and (fung? or antifung? or echinocandin b or ecb)

L30 0 FILE MEDLINE
L31 1 FILE CAPLUS
L32 0 FILE BIOSIS
L33 0 FILE EMBASE
L34 1 FILE WPIDS

TOTAL FOR ALL FILES
L35 2 L29 AND (FUNG? OR ANTIFUNG? OR ECHINOCANDIN B OR ECB)

=> dup rem l35

PROCESSING COMPLETED FOR L35
L36 2 DUP REM L35 (0 DUPLICATES REMOVED)

=> d cbib abs 1-2 hit

L36 ANSWER 1 OF 2 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
AN 2000-237849 [20] WPIDS
AB WO 200012540 A UPAB: 20000426
NOVELTY - A **reversible** peptide adduct comprising a boric or **boronic acid** complexed with a 1,2-cis-diol **cyclic-peptide**, which is more water soluble then the parent 1,2-cis-diol **cyclic peptide**, and its preparation, are new.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:
(1) a method for forming a **reversible cyclic peptide** adduct, comprising adding a 1,2-cis-diol **cyclic peptide** to an aqueous solution of a boric or **boronic acid**, then adjusting the pH of the solution to a value sufficient for complexation;
(2) a method of **purifying** a **cyclic peptide** having a 1,2-cis-diol moiety, comprising providing a crude mixture of a **cyclic peptide** having at least one

1,2-cis-diol functionality, complexing it with a boric or **boronic acid** to form a **reversible** adduct, solubilizing the adduct in aqueous solution, removing any insoluble material, acidifying the solution to a pH value no more than the pKa of the acid, and recovering the **cyclic peptide** from the solution;

(3) a method of **purifying** a 1,2-cis-diol **cyclic peptide**, comprising

(a) providing a crude mixture of a **cyclic peptide** having at least one 1,2-cis-diol functionality;

(b) complexing the functionality with a boric or **boronic acid** to form a **reversible** adduct;

(c) solubilizing the adduct in aqueous solution;

(d) concentrating the solution;

(e) absorbing the concentrate onto a **reverse**-phase hydrophobic resin packed in a chromatography column;

(f) eluting with an aqueous solvent system;

(g) combining the effluent fractions containing the adduct;

(h) acidifying the effluent solution to a pH no higher than the pKa of boric or **boronic acid**, to decomplex the adduct; and

(i) recovering the **cyclic peptide** from the acidified effluent solution; and

(4) a pharmaceutical formulation comprising a **reversible** adduct comprising a complex of a boric or **boronic acid** with a **cyclic peptide** having a 1,2-cis-diol moiety.

ACTIVITY - **Antifungal**.

MECHANISM OF ACTION - None given.

USE - The complexes are useful for **purification**, isolation, stabilization and/or water solubilization of the parent 1,2-cis diol **cyclic-peptide**, e.g. the increased solubility of the adduct allows the separation of the soluble adduct from other insoluble materials. (I) can be used to treat **fungal** infections.

Dwg.0/0

TI **Reversible** borate or boronate complexes of 1,2-cis-diol **cyclic-peptides**, useful for **purification**, isolation, stabilization and/or water solubilization of the parent 1,2-cis-diol **cyclic peptide**, and e.g. as **antifungal** agents.

AB WO 200012540 A UPAB: 20000426

NOVELTY - A **reversible** peptide adduct comprising a boric or **boronic acid** complexed with a 1,2-cis-diol **cyclic-peptide**, which is more water soluble then the parent 1,2-cis-diol **cyclic peptide**, and its preparation, are new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a method for forming a **reversible cyclic peptide** adduct, comprising adding a 1,2-cis-diol **cyclic peptide** to an aqueous solution of a boric or **boronic acid**, then adjusting the pH of the solution to a value sufficient for complexation;

(2) a method of **purifying** a **cyclic peptide** having a 1,2-cis-diol moiety, comprising providing a crude mixture of a **cyclic peptide** having at least one 1,2-cis-diol functionality, complexing it with a boric or **boronic acid** to form a **reversible** adduct, solubilizing the adduct in aqueous solution, removing any insoluble material, acidifying the solution to a pH value no more than the pKa of the acid, and recovering the **cyclic peptide** from the solution;

(3) a method of **purifying** a 1,2-cis-diol **cyclic peptide**, comprising

(a) providing a crude mixture of a **cyclic peptide**

having at least one 1,2-cis-diol functionality;
(b) complexing the functionality with a boric or **boronic acid** to form a **reversible** adduct;
(c) solubilizing the adduct in aqueous solution;
(d) concentrating the solution;
(e) absorbing the concentrate onto a **reverse**-phase hydrophobic resin packed in a chromatography column;
(f) eluting with an aqueous solvent system;
(g) combining the effluent fractions containing the adduct;
(h) acidifying the effluent solution to a pH no higher than the pKa of boric or **boronic acid**, to decomplex the adduct; and
(i) recovering the **cyclic peptide** from the acidified effluent solution; and
(4) a pharmaceutical formulation comprising a **reversible** adduct comprising a complex of a boric or **boronic acid** with a **cyclic peptide** having a 1,2-cis-diol moiety.
ACTIVITY - **Antifungal**.
MECHANISM OF ACTION - None given.
USE - The complexes are useful for **purification**, isolation, stabilization and/or water solubilization of the parent 1,2-cis diol **cyclic-peptide**, e.g. the increased solubility of the adduct allows the separation of the soluble adduct from other insoluble materials. (I) can be used to treat **fungal** infections.
Dwg.0/0

TECH UPTX: 20000426
TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred composition: The pharmaceutical composition further comprises and inert carrier, preferably water, and a wetting agent, lubricating agent, emulsifier, suspending agent, preservative, sweetner, stabilizer, perfuming agent, flavoring agent or a combination of them.

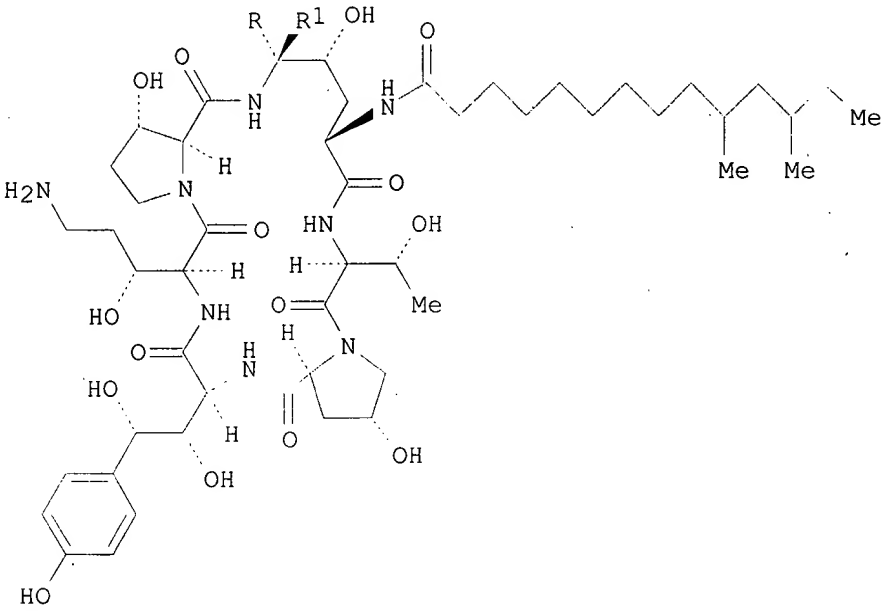
TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred Compounds: The **boronic acid** is an **alkylboronic acid**, heterocycloalkyl **boronic acid**, **arylboronic acid** or **heteroarylboronic acid**, e.g. **ethylboronic acid**, p **methoxyphenylboronic acid**, thiophene-2-**boronic acid** or indole-5 **boronic acid**. The adduct is preferably of an Echinocandin-type compound, and is of formula (I):
R = OH, alkoxy, phenoxy, alkl, phenyl, thiol, thioalkyl or thiophenyl;
R1 = H or C(O)R1a;
R1a = alkyl, alkenyl, alkynyl, aryl or heteroaryl;
R2 = H or Me;
R3 = H, Me, -CH2CONH2 or -CH2CH2NH2;
R4 = H or OH;
R5 = OH, -OPO3H2 or -OSO3H;
R6 = H or -OSO3H;
R7 = undefined;
X+ = a cation.
Preferred method: In the preparation method, the pH is adjusted in the range 7.5-9.5.

TT TT: **REVERSE** BORATE BORONATE COMPLEX CIS DIOL CYCLIC USEFUL **PURIFICATION** ISOLATE WATER PARENT CIS DIOL **CYCLIC PEPTIDE ANTIFUNGAL** AGENT.

L36 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2000 ACS
1996:580262 Document No. 125:222461 Preparation of novel **antifungal** cyclohexapeptides. Bouffard, Frances A. (Merck and Co., Inc., USA). PCT Int. Appl. WO 9622784 A1 19960801, 85 pp. DESIGNATED STATES: W: AL, AM, AU, AZ, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, IS, JP, KG, KR, KZ,

LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TM, TR, TT, UA, US, UZ, VN, AZ, BY, KG, KZ, RU; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1996-US921 19960122. PRIORITY: US 1995-378687 19950126.

GI



I

AB Novel carba cyclohexapeptide compds., e.g. (I.2HCl; R = CH2NH2, R1 = H) (I-A), which are useful as **antifungal** agents, in particular for the treatment of Pneumocystis carinii infections in immuno-compromised patients susceptible to infection, such as those suffering form AIDS, are prepd. Thus, 0.4 mL CF3CO2H was added to a soln. of 22.9 g I.HCl (R = OH, R1 = H) and 47.9 g H2NCH2CH2SH.HCl in 100 mL DMF and heated at 60.degree. for 4 h to give a mixt. of 6.5 g nor-thioether I.2CF3CO2H (R = H2NCH2CH2S, R1 = H) and 6.8 g epi-thioether I.2CF3CO2H (R = H, R1 = H2NCH2CH2S). The epi-thioether (6.5 g) was oxidized with 3.1 OXONE in MeCN/H2O at 25.degree. for 15 min to give the crude sulfone I.2CF3CO2H (R = H, R1 = H2NCH2CH2SO2) (73% purity), which was stirred with 0.5 M LiCN in DMF for 15 min to give 21% nor-nitrile I.2CF3CO2H (R = cyano, R1 = H) and 36% epi-nitrile I.2CF3CO2H (R = H, R1 = cyano). The nor-nitrile (283 mg) was reduced by 91.2 mg NaBH4 in the presence of 115 mg COCl2.6H2O in MeOH, treated with 2 N aq. CF3CO2H, and then **purified** by a column of Bio-Rad AG2-X8 (Cl-) resin to give I-A. I-A in vitro showed min. **fungicidal** concn. of <0.06, <0.06, and 0.25 .mu.g/mL against Candida albicans (MY1055), C. tropicalis (MY1012), and C. glabrata (MY1381), resp., and in vivo reduced P. carinii cysts in 5 rats by at least 90% when dosed at 0.02 mg/kg with all rats surviving.

TI Preparation of novel **antifungal** cyclohexapeptides

AB Novel carba cyclohexapeptide compds., e.g. (I.2HCl; R = CH2NH2, R1 = H) (I-A), which are useful as **antifungal** agents, in particular for the treatment of Pneumocystis carinii infections in immuno-compromised

patients susceptible to infection, such as those suffering form AIDS, are prepd. Thus, 0.4 mL CF3CO2H was added to a soln. of 22.9 g I.HCl (R = OH, R1 = H) and 47.9 g H2NCH2CH2SH.HCl in 100 mL DMF and heated at 60.degree. for 4 h to give a mixt. of 6.5 g nor-thioether I.2CF3CO2H (R = H2NCH2CH2S, R1 = H) and 6.8 g epi-thioether I.2CF3CO2H (R = H, R1 = H2NCH2CH2S). The epi-thioether (6.5 g) was oxidized with 3.1 OXONE in MeCN/H2O at 25.degree. for 15 min to give the crude sulfone I.2CF3CO2H (R = H, R1 = H2NCH2CH2SO2) (73% purity), which was stirred with 0.5 M LiCN in DMF for 15 min to give 21% nor-nitrile I.2CF3CO2H (R = cyano, R1 = H) and 36% epi-nitrile I.2CF3CO2H (R = H, R1 = cyano). The nor-nitrile (283 mg) was reduced by 91.2 mg NaBH4 in the presence of 115 mg COCl2.6H2O in MeOH, treated with 2 N aq. CF3CO2H, and then **purified** by a column of Bio-Rad AG2-X8 (Cl-) resin to give I-A. I-A in vitro showed min. **fungicidal** concn. of <0.06, <0.06, and 0.25 .mu.g/mL against Candida albicans (MY1055), C. tropicalis (MY1012), and C. glabrata (MY1381), resp., and in vivo reduced P. carinii cysts in 5 rats by at least 90% when dosed at 0.02 mg/kg with all rats surviving.

ST **antifungal** cyclohexapeptide prepn; Pneumocystis carinii infection AIDS

IT Acquired immune deficiency syndrome
(Pneumocystis carinii infection; prepn. of **antifungal** cyclohexapeptides)

IT Pneumocystis carinii
(infection in AIDS patients; prepn. of **antifungal** cyclohexapeptides)

IT Aspergillus
Candida albicans
Candida glabrata
Candida tropicalis
Fungicides and **Fungistats**
(prepn. of **antifungal** cyclohexapeptides)

IT Peptides, preparation
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(cyclohexa-, prepn. of **antifungal** cyclohexapeptides)

IT 181359-13-7P 181492-34-2P
RL: BPN (Biosynthetic preparation); PUR (Purification or recovery); RCT (Reactant); BIOL (Biological study); PREP (Preparation)
(deacylation product of N-(dimethyltetradecanoyl)cyclohexapeptide deriv. with Pseudomonas acidovorans; prepn. of **antifungal** cyclohexapeptides)

IT 181358-43-0P 181358-46-3P 181358-49-6P 181358-51-0P 181358-54-3P
181358-57-6P 181358-59-8P 181358-61-2P 181358-64-5P 181358-66-7P
181358-67-8P 181358-69-0P 181358-70-3P 181358-73-6P 181358-74-7P
181358-75-8P 181358-76-9P 181358-77-0P 181358-79-2P 181358-84-9P
181492-27-3P 181492-28-4P 181492-29-5P
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of **antifungal** cyclohexapeptides)

IT 74-88-4, Iodomethane, reactions 110-53-2, n-Pentyl bromide 156-57-0, 2-Aminoethanethiol hydrochloride 771-61-9, Pentafluorophenol 1184-90-3, Aminoiminomethanesulfonic acid 2408-36-8, Lithium cyanide **5419-55-6**, Triisopropyl borate 13795-24-9 16748-79-1 29558-77-8, 4-(4-Bromophenyl)phenol 53844-02-3 106359-65-3, 6-Octyloxy-2-naphthoic acid **135575-42-7**, Pneumocandin B0 **150167-55-8**
RL: RCT (Reactant)

(prepn. of **antifungal** cyclohexapeptides)
IT 63619-51-2P **150167-64-9P 150336-33-7P**
158937-25-8P 160430-94-4P 161216-99-5P 179463-15-1P
179463-16-2P 179463-18-4P 181359-02-4P 181359-09-1P 181359-11-5P
181359-16-0P 181359-19-3P 181359-21-7P 181359-24-0P 181359-27-3P
181359-29-5P 181359-32-0P 181492-30-8P 181492-31-9P 181492-32-0P
181492-33-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. of **antifungal** cyclohexapeptides)

=> dis his

(FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, WPIDS' ENTERED AT 15:27:24 ON 27 JUN 2000)
DEL HIS Y

FILE 'REGISTRY' ENTERED AT 15:35:12 ON 27 JUN 2000
L1 STR
L2 0 S L1
L3 0 S L1 FUL
L4 STR L1
L5 0 S L4
L6 0 S L4 FUL
L7 STR L1
L8 1 S L7
L9 14 S L7 FUL
L10 6002 S ?BORONIC ACID?/CNS
L11 5385 S ?BORIC ACID?/CNS
L12 23113 S CYCLIC PEPTIDE
L13 15 S CYCLO PEPTIDE

FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, WPIDS' ENTERED AT 15:46:09 ON 27 JUN 2000

FILE 'REGISTRY' ENTERED AT 15:46:19 ON 27 JUN 2000
L14 23113 S L12 OR L12
L15 9000 S L14 RAN=(128481-41-4,)
L16 9001 S L14 RAN=(78806-26-5,128481-41-4)
L17 5114 S L14 RAN=(,78806-26-5)

FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, WPIDS' ENTERED AT 15:47:09 ON 27 JUN 2000
L18 6 FILE MEDLINE
L19 74 FILE CAPLUS
L20 8 FILE BIOSIS
L21 19 FILE EMBASE
L22 3 FILE WPIDS
TOTAL FOR ALL FILES
L23 110 S (L10 OR L11 OR ?BORONIC ACID? OR ?BORIC ACID?) AND (L15 OR L1
L24 1 FILE MEDLINE
L25 14 FILE CAPLUS
L26 0 FILE BIOSIS
L27 0 FILE EMBASE
L28 1 FILE WPIDS
TOTAL FOR ALL FILES
L29 16 S L23 AND (PURIF? OR REVERS?)
L30 0 FILE MEDLINE
L31 1 FILE CAPLUS

```
L32             0 FILE BIOSIS
L33             0 FILE EMBASE
L34             1 FILE WPIDS
     TOTAL FOR ALL FILES
L35             2 S L29 AND (FUNG? OR ANTIFUNG? OR ECHINOCANDIN B OR ECB)
L36             2 DUP REM L35 (0 DUPLICATES REMOVED)

=> s l29 not l35

L37             1 FILE MEDLINE
L38            13 FILE CAPLUS
L39             0 FILE BIOSIS
L40             0 FILE EMBASE
L41             0 FILE WPIDS

TOTAL FOR ALL FILES
L42            14 L29 NOT L35

=> dup rem l42

PROCESSING COMPLETED FOR L42
L43            14 DUP REM L42 (0 DUPLICATES REMOVED)

=> d cbib abs 1-14


L43  ANSWER 1 OF 14  CAPLUS  COPYRIGHT 2000 ACS
2000:161314   Document No. 132:208137  Reversible boronate complexes
     of 1,2-cis-diol cyclic peptides.  Moser, Brian Allen;
     Baker, Jeffrey Clayton (Eli Lilly and Company, USA).  PCT Int. Appl. WO
     2000012540 A1 20000309, 35 pp.  DESIGNATED STATES: W:  AE, AL, AM, AT,
AU,
     AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI,
     GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
     LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU,
     SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW,
     AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI,
     CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL,
     PT, SE, SN, TD, TG.  (English).  CODEN: PIXXD2.  APPLICATION: WO
     1999-US19066 19990818.  PRIORITY: US 1998-98267 19980828.
GI
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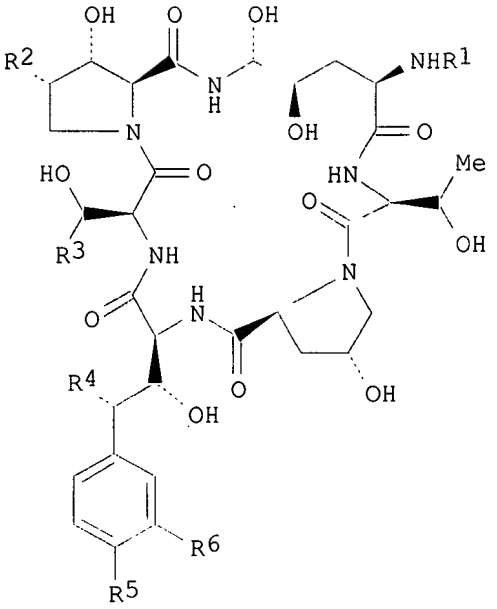

I

AB **Reversible** borate or boronate complexes of 1,2-cis-diol **cyclic peptides** are useful for **purifn.**, isolation, stabilization and/or water solubilization of their resp. parent 1,2-cis-diol **cyclic peptides** I (R1 = H, acyl; R2 = H, Me; R3 = H, Me, CH2CONH2, CH2CH2NH2; R4 = H, OH; R5 = OH, OPO3H2, OSO3H; R6 = H, OSO3H). The method is particularly useful for forming boronate adducts of hydrophobic echinocandin compds. to increase their water soly. Thus, the soly. of I (R1 = p-pentyloxy-p-terphenylcarbonyl; R2, R3 = Me; R4, R6 = H; R5 = OH) was increased in the presence of m-**aminophenylboronic acid** (concn. 23.76 mg/mL in supernatant or 94% of the original suspension, vs. 2.27 mg/mL in ammonium bicarbonate control supernatant).

L43 ANSWER 2 OF 14 CAPLUS COPYRIGHT 2000 ACS

1999:126126 Document No. 130:308549 Optode Membrane for Determination of Nicotine via Generation of Its Bromoethane Derivative. Choi, Martin M. F.; Wu, Xiao Jun; Li, You Rong (Department of Chemistry, Hong Kong Baptist University, Kowloon Tong, Peop. Rep. China). Anal. Chem., 71(7), 1342-1349 (English) 1999. CODEN: ANCHAM. ISSN: 0003-2700. Publisher: American Chemical Society.

AB A plasticized poly(vinyl chloride) optode membrane incorporated with a valinomycin ionophore, a H+-selective chromoionophore (ETH 5294), and a lipophilic potassium tetrakis(4-chlorophenyl)borate was used as a **reversible** sensing device for the indirect optical detn. of nicotine. Nicotine was extd. from a tobacco product (1-5 g) and converted to its bromoethane deriv. (NBD+Br-) by reacting with a soln. of bromoethane in ethanol. NBD+Br- in a soln. of 0.05M **boric acid**-Borax buffer and 0.2 mM Triton X-100 was extd. into the bulk of the membrane and subsequently caused changes in optical absorption of the sensing layer. The response slope, dynamic working range, detection limit, sensitivity, selectivity, effects of buffer soln. and neutral surfactant Triton X-100, and lifetime were discussed. The response was pH

dependent. At pH 8.5, the detection range was extended from 0.4 .mu.M to 1 mM. Typical response times (t95) of the samples were 2-4 min. The optode method was successfully used to detect nicotine in a tobacco sample from the market (av. content 0.720%; relative std. deviation 0.044%; n = 11). The interference of K+ on the optode method can be prevented by the pre-extn. procedure. Malic acid and citrate showed no interferences. The recovery of nicotine as NBD+ was 84-119% in the range 0.035-5% nicotine. The result was satisfactory compared with an AOAC UV std. method.

L43 ANSWER 3 OF 14 MEDLINE

1999416193 Document Number: 99416193. Analysis of leptin gene expression in chickens using **reverse** transcription polymerase chain reaction and capillary electrophoresis with laser-induced fluorescence detection. Richards M P; Ashwell C M; McMurtry J P. (US Department of Agriculture, Livestock and Poultry Sciences Institute, Beltsville, MD 20705-2350, USA.. richards@lpsi.barc.usda.gov) . JOURNAL OF CHROMATOGRAPHY. A, (1999 Aug 20) 853 (1-2) 321-35. Journal code: BXJ. Pub. country: Netherlands. Language: English.

AB Leptin is a peptide hormone product of the obese (ob) gene that functions in the regulation of appetite, energy expenditure and reproduction in animals and humans. We have developed a technique using capillary electrophoresis with laser-induced fluorescence detection (CE-LIF) for the analysis of chicken leptin (261 base pairs, bp) and beta-actin (612 bp) double-stranded DNA products from **reverse** transcription polymerase chain reaction (RT-PCR) assays. Amplicons were separated using a DB-1 coated capillary (27 cm x 100 microns I.D.) at a field strength of 300 V/cm in a replaceable sieving matrix consisting of 0.5% hydroxypropylmethylcellulose (HPMC) in 1X TBE (89 mM Tris-base, 89 mM **boric acid**, 2 mM EDTA, pH 8.3) buffer with 0.5 microgram/ml EnhanCE fluorescent intercalating dye. RT-PCR samples (1-2 microliters) were diluted 1:100 with deionized water and introduced into the capillary by electrokinetic injection. Separations were completed in less than 6 min and the total time required per sample, including capillary conditioning, was 8 min. We have applied RT-PCR-CE-LIF to determine the effects of insulin and estrogen treatment on leptin gene expression relative to that of beta-actin in chicken liver and adipose tissue. In addition, we have constructed a chicken leptin mRNA competitor (234 bp amplicon) and evaluated it for use as an internal standard in the development of a quantitative-competitive RT-PCR assay. Our findings represent the first reported application of capillary electrophoresis to the analysis of leptin gene expression by RT-PCR.

L43 ANSWER 4 OF 14 CAPLUS COPYRIGHT 2000 ACS

1998:564012 Document No. 129:336870 The direct electrochemistry of N-acetyl-microperoxidase-8 in aqueous and dimethyl sulfoxide solution. Ci

Li, Qui; Mabrouk, Patricia Ann (Department of Chemistry, Northeastern University, Boston, MA, 02115, USA). J. Electroanal. Chem., 455(1-2), 45-48 (English) 1998. CODEN: JECHES. ISSN: 0368-1874. Publisher: Elsevier Science S.A..

AB The direct electrochem. of N-acetyl-microperoxidase-8 (N-Ac-MP-8) at naked Pt has been investigated in both aq. and DMSO soln. using cyclic voltammetry. In both aq. and non-aq. media, heterogeneous electron transfer has been found to be persistent and at least quasi-

reversible. The aq. redox potential for N-Ac-MP-8 (-169.+-.5 mV vs. SHE) is consistent with recent studies establishing that at high ionic strength in aq. buffered solns. the heme peptide is a low-spin six-coordinate complex in which water occupies the sixth axial ligand site. The redox potential at Pt in DMSO solns. (<0.1% H2O), +103.+-.5 mV vs. SHE, is in the range of redox potentials typically obsd. for type II cytochromes c in which the sixth axial ligand binding site is vacant.

L43 ANSWER 5 OF 14 CAPLUS COPYRIGHT 2000 ACS
1997:734740 Document No. 127:322728 Stability of octastatin, a somatostatin analog cyclic octapeptide, in aqueous solution. Jang, Sun Woo; Woo, Byung Ho; Lee, Jung Tae; Moon, Seung Cheol; Lee, Kang Choon; DeLuca, Patrick P. (Drug Targeting Laboratory, College of Pharmacy, SungKyunKwan University, Suwon City, 440-746, S. Korea). Pharm. Dev. Technol., 2(4), 409-414 (English) 1997. CODEN: PDTEFS. ISSN: 1083-7450. Publisher: Dekker.

AB The degrdn. of octastatin, a cyclic octapeptide analog of somatostatin, was examd. as a function of pH, temp., buffer, and ionic strength by **reversed**-phase gradient high-performance liq. chromatog. Degrdn. of octastatin followed a first-order kinetics. Various buffer species such as acetate, ammonium acetate, citrate, glutamate, phosphate, and borate showed differing effects on the degrdn. of the octapeptide. Good stability was found in glutamate and acetate buffer of pH 4.0. Degrdn. of octastatin was greater in citrate- or phosphate-contg. buffers than in glutamate or acetate buffers. With phosphate buffer, higher buffer concn. caused greater degrdn., while in acetate buffer, the effect of buffer concn. and ionic strength was negligible. In addn., the degrdn. of octastatin was markedly inhibited by increasing the concn. of glutamate buffer. This study allows the prediction of good stability in acetate buffer (0.01 M, pH 4.0) with a t90% of 84.1 days at 20.degree.C.

L43 ANSWER 6 OF 14 CAPLUS COPYRIGHT 2000 ACS
1996:434961 Document No. 125:76328 Active agent transport systems using perturbants to convert active agent to state between native and denatured states. Milstein, Sam J.; Barantsevitch, Evgueni; Leone-Bay, Andrea; Wang, Nai Fang; Sarubbi, Donald J.; Santiago, Noemi B. (Emisphere Technologies, Inc., USA). PCT Int. Appl. WO 9612475 A1 19960502, 119 pp. DESIGNATED STATES: W: AL, AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MK, MN, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1995-US14598 19951024. PRIORITY: US 1994-328932 19941025.

AB Methods are disclosed for transporting a biol. active agent across a cellular membrane or a lipid bilayer. A first method includes the steps of: (a) providing a biol. active agent which can exist in a native conformational state, a denatured conformational state, and an intermediate conformational state which is **reversible** to the native state and which is conformationally between the native and denatured states; (b) exposing the biol. active agent to a complexing perturbant to **reversibly** transform the biol. active agent to the intermediate state and to form a transportable supramol. complex; and (c) exposing the membrane or bilayer to the supramol. complex, to transport the biol. active agent across the membrane or bilayer. The perturbant has a mol. wt. between about 150 and about 600 daltons, and contains at least one hydrophilic moiety and at least one hydrophobic moiety. The supramol.

complex comprises the perturbant noncovalently bound or complexed with the biol. active agent. In the present invention, the biol. active agent does not form a microsphere after interacting with the perturbant. A method for prepg. an orally administrable biol. active agent comprising steps (a) and (b) above is also provided as are oral delivery compns. Addnl., mimetics and methods for prepg. mimetics are contemplated. The methods and compns. of the invention facilitate the delivery of an active agent to a target, e.g. the delivery of a pharmaceutical through an adverse environment to a particular location in the body. The biol. active agent may be e.g. a carbohydrate, mucopolysaccharide, lipid, pesticide, or peptide, e.g. human or bovine growth hormone, an interferon, insulin, an antigen, a monoclonal antibody, cromolyn sodium, vancomycin, heparin, etc. The perturbant may be e.g. a proteinoid, carboxylic acid, or acylated amino acid or poly(amino acid). The perturbant may also be a pH-changing agent, an ionic strength-changing agent, or guanidine-HCl.

L43 ANSWER 7 OF 14 CAPLUS COPYRIGHT 2000 ACS

1996:672984 Document No. 126:19213 Total Synthesis of the Serine-Threonine Phosphatase Inhibitor Microcystin-LA. Humphrey, John M.; Aggen, James B.; Chamberlin, A. Richard (Department of Chemistry, University of California, Irvine, CA, 92717, USA). J. Am. Chem. Soc., 118(47), 11759-11770 (English) 1996. CODEN: JACSAT. ISSN: 0002-7863. OTHER SOURCES: CASREACT 126:19213. Publisher: American Chemical Society.

AB **Reversible** protein phosphorylation, which is mediated by kinases and phosphatases, is a major control element of the cell. There is a diverse group of toxic natural products that inhibit certain phosphatases, thereby disrupting normal biochem. pathways. These toxins can be useful for dissecting the individual biochem. pathways assocd. with each of these enzymes. This article describes the first total synthesis of one such toxin, the cyclic heptapeptide microcystin-LA. The synthesis features a convergent route that is amenable to analog prepn. in the search for selective phosphatase inhibitors. A new route to the unusual amino acid Adda is described, which incorporates an efficient diastereoselective aspartate alkylation and diene synthesis via a Suzuki coupling reaction. This work also features an efficient prepn. of an N-methylalanine contg. peptide via a Horner-Emmons condensation and several difficult amino acid coupling reactions that relied heavily on Carpino's remarkable HATU reagent.

L43 ANSWER 8 OF 14 CAPLUS COPYRIGHT 2000 ACS

1995:86935 Document No. 122:4030 Affinity chromatography of proteolytic enzymes. Rudenskaya, G. N. (M. V. Lomonosov Moscow State Univ., Dep. Chem., Russia). Bioorg. Khim., 20(3), 213-28 (Russian) 1994. CODEN: BIKHD7. ISSN: 0132-3423.

AB A review with 70 refs. on the affinity chromatog. of proteinases as the most efficient approach to their sepn. are reviewed. The paper contains discussion of the methods used to prep. affinity sorbents by attaching gramicidin and bacitracin to various supports. The two cyclopeptides contain amino acid residues, meeting specificity requirements of proteinases of various classes, these materials thus being affinity sorbents of general type. Rules governing the interaction of proteinases

with these sorbents are discussed, along with numerous examples of their chromatog. on sorbents of general type as well as on more specific sorbents adapted to the sepn. of particular types of proteinases. Sorbents contg. benzylsuccinic, benzylmalonic and **phenylboronic acid** residues are considered in details.

L43 ANSWER 9 OF 14 CAPLUS COPYRIGHT 2000 ACS
1994:417812 Document No. 121:17812 A self-regulated insulin delivery system using **boronic acid** gel. Shiino, D.; Kataoka, K.; Koyama, Y.; Yokoyama, M.; Okano, T.; Sakurai, Y. (Int. Cent. Biomater. Sci., Noda, 278, Japan). Proc. Int. Conf. Intell. Mater., 1st, 301-4. Editor(s): Takagi, Toshinori. Technomic: Lancaster, Pa. (English) 1993. CODEN: 59CBA5.
AB A novel polymer system sensitive to glucose concn. have been studied as a candidate material for chem. regulate insulin release system. Ph **boronic acid** is capable to form **reversible** binding to cis-diol substances. Glucose responsive insulin release system has been studied with utilization of **boronic acid** polymers for the key material to exchange reaction between gluconic acid modified insulin and glucose mol. The released concn. of gluconic acid modified insulin from the polymer was pulsatile in response to the repeated stepwise concn. changes of glucose. Another remarkable result is that the release response have no lag time to change of glucose concn. The **boronic acid** polymer shows considerable promise for use in a self-regulating insulin delivery system.

L43 ANSWER 10 OF 14 CAPLUS COPYRIGHT 2000 ACS
1987:629300 Document No. 107:229300 On-line post-column fluorescence detection for N-terminal tyrosine-containing peptides in high-performance liquid chromatography. Ohno, Masahiro; Kai, Masaaki; Ohkura, Yosuke (Fac. Pharm. Sci., Kyushu Univ., Fukuoka, 812, Japan). J. Chromatogr., 421(2), 245-56 (English) 1987. CODEN: JOCRAM. ISSN: 0021-9673.
AB A detection system based on online post-column fluorescence derivatization is described for the detn. of N-terminal tyrosine-contg. peptides by **reversed**-phase HPLC. The peptides are automatically converted into fluorescent derivs. by reaction with hydroxylamine, Co(II), and borate after peptide sepn. on a **reversed**-phase column (TSKgel ODS-120T) followed by passage through an UV absorbance detector. The reaction system permits the fluorescence detection at 435 nm (emission) with excitation at 335 nm for N-terminal tyrosine-contg. synthetic peptides in as little as picomole amts. The facile fluorescence detection of N-terminal tyrosine-contg. fragments produced from methionine-enkephalin by enzymic degrdn. in a rat brain homogenate was achieved by comparison with the UV absorption detection at 215 nm.

L43 ANSWER 11 OF 14 CAPLUS COPYRIGHT 2000 ACS
1981:438127 Document No. 95:38127 **Purification** of proteolytic enzymes. Stepanov, V. M.; Rudenskaya, G. N.; Akparov, V. K.; Gaida, A. V. (USSR). U.S. US 4264738 19810428, 7 pp. (English). CODEN: USXXAM. APPLICATION: US 1979-62683 19790801.
AB Proteolytic enzymes are **purified** by specific sorption on activated aminosilica covalently bonded with a class-specific ligand (gramicidin S, bacitracin, bacilliquine, or **phenylboric acid**). Thus, bacitracin-silochrome (contg. 46 .mu.mol of bactracin/g dry sorbent) was prepd. by mixing 1 g of aminosilochrome with

34 mg of p-benzoquinone, and 220 mg of bacitracin, stirring, and overnight
incubation at 5.degree.. A soln. contg. pig pepsin was applied to a column contg. the sorbent in 0.1M AcOH, pH 5.0. Pepsin (**purified** 1.5-fold) was eluted with 25% iso-PrOH in 1M NaCl, pH 5.0 in a 100% yield.

L43 ANSWER 12 OF 14 CAPLUS COPYRIGHT 2000 ACS
1980:634017 Document No. 93:234017 **Purification** of proteolytic enzymes. Gaida, A. V.; Stepanov, V. M.; Akparov, V. K.; Rudenskaya, G. N.
(All-Union Scientific-Research Institute of Genetics and Selection of Industrial Microorganisms, USSR; Moscow State University). Brit. UK Pat. Appl. GB 2031432 19800423, 11 pp. (English). CODEN: BAXXDU. PRIORITY: SU 1978-2649412 19780725.
AB Proteolytic enzymes were **purified** by affinity chromatog. on the reaction product of an amino deriv. of a siliceous material with a ligand and a condensation agent. E.g., bacitracin-silochrome was prepd. by reaction of aminosilochrome with p-benzoquinone and bacitracin, and a column of this sorbent was used for affinity chromatog. **purifn.** of crude proteinase. A 1.5-fold **purifn.** was obtained with a 100% yield in terms of activity.

L43 ANSWER 13 OF 14 CAPLUS COPYRIGHT 2000 ACS
1967:489941 Document No. 67:89941 **Reversing** the morphogenetic effect of **phenylboric acid** and of the lanceolate gene with actinomycin D in the tomato. Mathan, David S. (California Inst. of Technol., Pasadena, Calif., USA). Genetics, 57(1), 15-23 (English) 1967. CODEN: GENTAE.
AB Actinomycin D (I) (100 .mu.g./ml.) increased the size of the first tomato leaf of normal form (pinnately compd. leaf) (La+/La+) and of the mutant lanceolate form (La+/La) when given on the 3rd day of the germination for 3-5 days. Assocd. with the increase in leaf size was a redn. in activity of tyrosinase, laccase, and catalase. I **reversed** the effect of **phenylboric acid** (II) with respect to both the size and shape of the leaf, and **reversed** the activity of the 3 enzymes. II (30 .mu.g./ml.) applied to La+/La+ seeds for the 1st 24 hrs. of germination transformed the 1st true leaf of the seedling from a compd. leaf to a lanceolate leaf. If, however, on the 3rd day of germination following the II treatment, the seedlings were placed in a soln. of 50-100
actinomycin D/ml. for 3-4 days, the transformation of the first true leaf to a typical lanceolate leaf did not occur; instead, 25% of the seedlings showed a normal 1st leaf, and the rest ranged in shaped and size from normal to an enlarged lanceolate leaf. It has been shown that treatment of La+/La+ or La+/La seeds with 300 .mu.g. II/ml. in the 1st 24 hrs. of germination caused an increase in the level of activity of tyrosinase, laccase, peroxidase, and catalase. However, if 2 days after II treatment the seedlings were placed in 50-100 .mu.g. I/ml. soln. and kept in the dark for an addnl. 3-5 days, the level activity of tyrosinase, laccase, and catalase was considerably below that of seedlings treated with II alone. 15 references.

L43 ANSWER 14 OF 14 CAPLUS COPYRIGHT 2000 ACS
1967:1346 Document No. 66:1346 Spasmolytic activity of pentaerythritol bis(p-methylphenyl) boronate. Pham-Huu-Chanh; Pene, A. M.; Cheav-Seang-Lean (C.N.R.S., Toulouse, Fr.). Agressologie, 7(5), 501-6 (French) 1966. CODEN: AGSOA6.
AB Pentaerythritol bis(p-methylphenyl) boronate (I) was spasmolytic towards induced contractions of the isolated rabbit jejunum, guinea pig duodenum, and the rat uterus. I was active on the jejunum at a 5 .times. 10-7

g./ml. concn.; repeated applications and washings completely and irreversibly abolished contraction. The spasmolytic effect on the duodenal and uterine prepns. was **reversible** after washing, even after application of concns. as high as 4 .times. 10-4 g./ml. The antispasmodic effects were of both musculotropic and neurotropic origin; spasmolytic activity of I was apparently produced through a papaverinetype mechanism. I also showed activity against histamine, oxytocin, and esp. against serotonin; there may be a correlation between the antiserotonin and psychotropic activities of the compd.

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